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IN MEMORIAM

FRANKLIN H. MARTIN
1857-1935

FRANKLIN H. MARTIN, friend, dreamer, idealist, among the greatest in medicine, died quietly on March 7, 1935, in Phoenix, Arizona. Born in Ixonia, Wisconsin, on July 13, 1857, of pioneer stock, Franklin Martin remained, throughout his long and constructive life, a pioneer in medicine, a teacher and an organizer.

His education at the rural public schools in Wisconsin was haphazard, and often interrupted because of the adverse fortunes of his family, and Frank Martin, as a young boy, began devising ways to supplement the family income: weeding gardens, herding sheep, chopping wood, helping with the haying, making bricks, or whatever came to hand. The education he got he more than earned, and what he learned stuck with him, in spite of the many moves from place to place, from one crude school to another. In 1876, while working on a farm, he decided suddenly that, in spite of the obvious hardships this would entail, he would "be a Doctor," and so, the following fall, he attached himself to Dr. William C. Spalding in Watertown, Wisconsin, to read and study. There he met and formed a friendship with Frederick Parkhurst, who likewise was studying under a local physician, and these two young men, nothing daunted by their poverty, decided to enter the Chicago Medical College (now Northwestern University Medical School). So, in the fall of 1877, he embarked upon the rather hazardous, and certainly strenuous business of a medical course, and in 1880 Franklin Martin emerged with an M.D. degree. The year following his graduation he spent as an interne at the Mercy Hospital in Chicago.

From then on he became a teacher, educator and organizer, as well as entering private practice in the field of gynecology. His interests widened rapidly, and he published, from time to time, numerous papers

on gynecologic subjects. His tenacity in securing an education, and making a living while doing so, stood him in good stead as the years passed, as well as playing a large part in the winning of the charming Miss Hollister for his wife in 1886, in spite of the opposition of her parents. This same quality, as well as his perseverance, dynamic personality and tireless energy, aided him in drawing to him, and having cooperate with him, people who could and did serve him to the best of their ability. In 1888 he assisted in organizing the Post-Graduate Hospital School of Chicago.

The adage "The boy is father to the man," as Dr. George Crile points out in his foreword to *The Joy of Living*, seems especially apt in the case of Franklin Martin, for the boy, doggedly making bricks, soon matured into the man who laid many corner stones, and his first outstanding accomplishment was the establishment of *Surgery, Gynecology and Obstetrics* in 1905, to which, in 1913, was added the *International Abstracts of Surgery*. He edited this journal from the day of its inception to the time of his death. This first successful venture and its development led to the founding of the Clinical Congress of Surgeons of North America in 1910, and the founding of the American College of Surgeons in 1913. Later, in 1921, he founded and directed the Gorgas Memorial Institute of Tropical and Preventive Medicine.

As has often been pointed out, Franklin Martin's plans for the advancement of surgery could not have been so fruitful without the interest and cooperation of leaders in the field of surgery, but, here again, his power of attracting people and binding them to him, his vivid imagination, his fearlessness, his sincerity and faith, courage and determination, were all in his favor, and those who knew him well, and worked with him, trusted and believed in him. Probably no other man was more alive to the changing conditions in public institutions, more interested in political trends and social economics. He was ever on the alert for, and quick to recognize, trends which would be useful and practical for the improvement of the medical profession.

During the World War, in 1916, President Woodrow Wilson asked him to head the development of medical participation, and he became the Chairman of the General Medical Board of the Council of National Defense, and, again, it was he who was responsible for the development of the Volunteer Medical Service Corps. He served as a Colonel in the Medical Corps of the United States Army, and was with the American Expeditionary Forces for three months. He has left a valuable record of the work of the Medical Section of the Council of National Defense, published in book form in 1934.

The success of his leadership and organizational efforts brought him many honors and recognition from all over the world. He extended the influence of the American College of Surgeons to South American and European countries, and because of this work, he received the

honorary Fellowships and membership of many of them. He was given an LL.D. degree from Queen's University, Belfast, Ireland; from the University of Wales, Cardiff; from the University of Pittsburgh; the degree of D.Sc. from Northwestern University, and the degree of D.P.H. from Detroit College of Medicine and Surgery. He was decorated with the Companion Order of St. Michael and St. George by King George V of England in 1919, and received the Distinguished Service Medal of the United States Government, as well as the Order of Commander of the Crown of Italy.

His offices were too numerous to enumerate in detail, but, in addition to editing *Surgery, Gynecology and Obstetrics* for thirty years, he was active Director of the American College of Surgeons for twenty-two years. He was President of the American Gynecological Society; President of the American College of Surgeons in 1929; Trustee of Northwestern University from 1921 to 1931, and Chairman of the Board of the Gorgas Memorial Institute from 1921 to the time of his death. Dr. Martin accepted membership on the Advisory Editorial Board of this JOURNAL at the time of its founding and continued his interest in the publication up to the time of his death.

Franklin Martin also contributed several well-known articles and books to medical literature: "The Treatment of Fibroid Tumors of the Uterus"; "Treatise on Gynecology"; "South America From the Surgeon's Standpoint"; "Australia and New Zealand"; "The Joy of Living," an Autobiography, in two volumes, and "Digest of the Proceedings of the Council of National Defense During the World War."

Although Franklin Martin was a shy and reserved man, his various activities and contacts all over the world made him genial, cultured and well-informed. He was a man of distinguished appearance; one who dominated a group and stood out from it. His intelligence, kindness and charm made friends for him wherever he went, and there are eminent people from Australia to Hungary who will feel a great personal loss in the passing of Franklin Martin, who was as distinctly an individual as he was an organizer and leader of men.

C. Jeff Miller.

Original Communications

RENAL FUNCTION IN THE TOXEMIAS OF PREGNANCY*

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APPROXIMATELY 8 per cent of the patients delivered in a maternity hospital have toxemia. This is characterized clinically by the occurrence of one or more of the following signs: Hypertension, albuminuria, or edema. In addition, there may be symptoms of various visual disturbances (diplopia, scotomas, amaurosis), dizziness, epigastric pain, vomiting, or oliguria. The classical case of toxemia of pregnancy occurs in primiparas in whom the onset of symptoms is manifested in the last trimester, particularly in the last two to six weeks of pregnancy. The disease is termed preeclampsia, but if the patient has convulsions and/or coma in addition to one or more of the signs, it is called eclampsia. Apparently the condition subsides rapidly after delivery or death of the fetus, and leaves the patient with a normal cardiovascular-renal system. However, toxemia may recur in subsequent pregnancies, but the symptoms and signs will appear, as a rule, earlier than in the first pregnancy.

The recurrence or persistence of toxemia has been variously designated as chronic, recurrent or latent nephritis, recurrent toxemia of pregnancy, or low reserve kidney if there is no apparent increase in severity. DeSnoo and Adair were among the first obstetricians to add essential hypertension to the list. When these symptoms appear during pregnancy it is of the utmost importance to know as soon as possible whether the patient is suffering from preeclampsia, which probably will not recur in subsequent pregnancies, or whether she has a chronic nephritis or an essential hypertension. Both of these diseases are progressive and their courses are usually accelerated by the pregnancy. We have never observed a case of acute or chronic nephritis in which the patient improved during pregnancy, but have seen patients with hypertension and/or albuminuria in whom there was no perceptible increase in the disease during pregnancy.

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NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

The incidence of the toxemias of pregnancy for the Cornell University Clinic is 15.6 per cent and for the Johns Hopkins Clinic 9.4 per cent, as reported by Stander; Washington University Clinic, 3.8 per cent, according to Schwarz and Wegner, and 6.7 per cent for the University of Chicago Clinic. A conservative estimate of the number of patients with toxemia of pregnancy in the United States each year would be 100,000. Thus some idea is given of the importance of the toxemias of pregnancy to both the individual and to the race.

Innumerable reports have been published in the past fifty years, some confirming and others denying that permanent renal damage occurs in patients with pre-eclampsia or eclampsia. Reports from various German clinics indicate that permanent renal damage from eclampsia or preeclampsia is unusual, if not actually rare. Schultz, in 1932, in a follow-up study of 780 toxemic patients from 1900 to 1930, was able to examine 124. He found 13, or 10.5 per cent, with hypertension and/or albuminuria. In the same clinic, in 1925, Nevermann studied 60 patients who had had eclampsia or preeclampsia in the preceding twenty-five years, and found 14, or 23.4 per cent, with hypertension or albuminuria. Seven years later when these same 14 patients were seen by Schultz, their condition had not been made worse. Therefore, he concludes that the renal affections of eclampsia always heal and that the evolution into chronic nephritis is exceptional. It is usually possible to discover some other cause for renal disease in the history of such a patient.

There is lack of agreement among the British authors, but the majority believe that a considerable proportion of the patients with eclampsia or preeclampsia have resultant permanent renal damage.

Stander, Peckham, and Harris, in this country, state that from 20 to 75 per cent of the toxemic patients have evidence of chronic nephritis when examined one year later. There is no doubt that the occurrence of toxemia predisposes to a recurrence in subsequent pregnancies. Young and Sym state that from 40 to 45 per cent of the patients with eclampsia have some evidence of toxemia in subsequent pregnancies. We have noted in a series of 438 toxemic patients that 90, or 20 per cent, gave histories of previous toxemia. In 29 patients with histories of convulsions in previous pregnancies, 26, or 90 per cent, had some evidence of toxemia during the pregnancy under our observation.

An explanation of these conflicting reports may be found in the criteria used in making a diagnosis of nephritis. For the past twenty-five years a diagnosis of chronic nephritis was made by the obstetrician on the basis of the presence of hypertension, albuminuria, and/or edema if one or more of these signs (1) persisted for more than three weeks postpartum; (2) appeared in the first half of pregnancy, especially in multiparas; (3) recurred in subsequent pregnancies, or (4) if a history of nephritis or hypertension was obtained from the patient.

Such a classification was satisfactory for a time, but with knowledge gained by observations made on men, nonpregnant women, by various renal functional tests and postmortem examinations, it soon became evident that the diagnosis of chronic nephritis was not suitable in many cases. In some of them the only abnormal finding would be a hypertension, and the cause of death would be due to a hemorrhage, usually cerebral, rather than renal failure. These patients would be classified as having a primary or essential hypertension. In the other

group of patients who gave a history of acute glomerulonephritis with a possible exacerbation during pregnancy, or an acute toxemia of pregnancy of long duration, producing renal changes similar to those found after an acute nephritis, the classification would be chronic glomerulonephritis. The correct diagnosis is of importance to the physician because by clarifying the clinical and pathologic condition he is a step closer to the etiology, prevention, and cure. Furthermore, he will know better how to manage the pregnancy, the complications to be anticipated and how to prevent them, and whether or not the present pregnancy should be interrupted and future pregnancies prevented.

The internist requires a history of a typical acute attack of nephritis or symptoms and signs of kidney pathology, as well as evidence of renal impairment, before he will make a diagnosis of chronic glomerulonephritis. The German authors insist upon similar evidence but very few, if any, of the English or American obstetricians make this distinction. Undoubtedly, many of the toxemic patients who are classed as having chronic nephritis have hypertension as the principal sign, which may be caused or aggravated by the pregnancy. The blood pressure may either return to normal between pregnancies or remain permanently elevated, the latter occurring usually after repeated pregnancies. At the Johns Hopkins Clinic (Harris, Stander, Peckham) hypertension in pregnancy has never been recognized as a disease entity. While many of the patients with hypertension will ultimately have kidney damage, as proved by renal function tests and autopsy, the pathologist is unable, in some cases, to state whether the glomerulus was destroyed as a result of glomerulonephritis or nephrosclerosis. We believe, according to the data at hand, that an *increase in blood pressure* is usually the first, and ordinarily the most frequently encountered, sign of the recurrent toxemias of pregnancy.

Obstetricians long have spoken of the load produced by pregnancy on the cardiovascular-renal system, but never have been able to define just what it is. It certainly is not the metabolic waste products of the fetus since it manifests itself when the fetus is still small, in many instances only 8 or 10 cm. in length. We believe that the load is caused by the marked changes in the maternal metabolism produced by the pregnancy. Some of these changes are: (1) A tendency toward a positive water balance (edema); (2) a decrease in serum protein; (3) an alteration in the nitrogen, fat, carbohydrate, and mineral metabolism; (4) the congestion of many tissues and organs; (5) the increased permeability of vessel and cell walls; (6) the increased absorption of toxic substances from the intestines, and decreased elimination of waste products due to constipation, and (7) increased irritability of the central nervous system, etc.

These marked alterations in metabolism and physicochemical changes in the cell wall may place an additional strain on the vascular system and kidneys. However, the load imposed by pregnancy is demonstrated best, perhaps, by noting the rapid abatement of symptoms and signs in cardiac, nephritic, or toxemic patients subsequent to the termination of pregnancy at two to five months, long before there could be any mechanical factor because of the size of the fetus.

We have divided the patients into convulsive and nonconvulsive toxemia, the latter comprising the acute and chronic types. The patients with nonconvulsive toxemia have been divided as follows: Group I (acute or preeclamptic toxemia) consists of patients of whom the majority are primiparas, who have had normal pregnancies until the last trimester, when the symptoms and signs of toxemia developed. Group II comprises those patients who gave histories of previous toxemia of pregnancy, acute nephritis (rare), or hypertension. Group III includes multiparas in whom the past history has been negative. In another group we have listed the patients who had had abruptio placentae because of the reported frequency of chronic nephritis (recurrent toxemia) as a cause or the result of abruptio placentae, and the high incidence of cortical necrosis of the kidney reported in association with it.

METHOD

The patients were admitted to the hospital and kept in bed. An enema or mild cathartic was given, and after at least twenty-four hours (usually 48 or more) the renal function tests were performed. Food and fluids were stopped the night preceding the test at 6:00 P.M. The patient's bladder was emptied at 6:00 A.M. A catheter was inserted at 9:00 A.M. and left in place for two hours, specimens being taken at 9:00, 10:00, and 11:00 A.M. At 9:00 A.M. the patient was given a breakfast which consisted of fruit, toast, cereal, and 200 c.c. of water. No coffee, tea, or milk was given. The urine specimens were taken to the laboratory immediately, measured, and 10 c.c. of the 9:00 A.M. specimen were centrifuged at 1,200 r.p.m. for ten minutes. The volume of sediment was noted and 9.5 c.c. were discarded. The remainder was shaken up and a portion transferred either to a blood or a mold counting chamber, and the average number of formed elements per low power field was counted. The specific gravity was determined on all three specimens, either by the gravimetric method, using 10 or 25 c.c. amounts, or by a certified pycnometer. Blood was obtained at 10:00 A.M. and a Folin-Wu filtrate was made. Urea in both blood and urine was determined in the majority of cases by Leiboff's acid hydrolysis method. The nonprotein nitrogen and many other constituents were determined on all blood specimens. All urine specimens were tested for albumin by heat and acetic or sulphosalicylic acid. Ambulatory cases were catheterized only once to obtain a specimen suitable for microscopic examination and albumin determination. All of the microscopic examinations have been made by the author.

RESULTS

From 1925 to March 31, 1934, approximately 850 patients with moderate and severe nonconvulsive toxemia, and 82 with eclampsia have been studied. Various blood and urine examinations, renal function tests, and many other special examina-

tions have been made in these toxemic patients in an endeavor to determine (1) the severity of the condition, (2) some criteria for a prognostic guide, and (3) some means of classification. The various renal functional tests used have been the concentration: diuresis, phenolsulphonephthalein, MacLean's urea concentration, urea clearance, and creatinine filtration. A short summary of our findings with these various functional tests, and a complete report of the results with the urea clearance will be given. These data will demonstrate that in both normal and toxemic pregnancy there is some decrease (at times marked) in the figures for many of the renal functional tests, probably due to extrarenal rather than renal causes, because soon after delivery many of the various functional tests show marked increases.

In Table I we have given the number of patients, age, and parity for the various groups. All of the patients had very definite evidence of toxemia, and approximately 80 per cent are classified as having a moderate or severe toxemia, according to the criteria used by us. The increasing age and multiparity are of interest in Groups II and III, as compared with Group I. These figures would seem to indicate that the incidence of toxemia increased with the age and parity of the patient. In Group I, the age and multiparity of several patients are at variance with the usual case of preeclampsia, but the histories, course and changes in blood volume, as described by us previously, were typical for acute toxemia.

TABLE I

	NONCONVULSIVE TOXEMIA			ECLAMPSIA	ABRUPTIO PLACENTAE
	GROUP I PRE- ECLAMPSIA	II HISTORY OF TOXEMIA	III NO HISTORY OF TOXEMIA		
<i>Age:</i>					
Minimum	18	19	24	16	24
Maximum	40	43	46	40	42
Average	26.4	31.9	34.3	25.9	33
<i>Parity:</i>					
Minimum	1	1	1	1	1
Maximum	8	15	13	9	14
Average	1.73	4.1	5.4	1.9	7
<i>Primiparas:</i>					
Number of cases	35	4		20*	7*
Total cases	46	58	38	26	24

*Eclampsia occurred in the first pregnancy in 20 patients, and abruptio placentae in 7.

The concentration-diuresis test is the simplest, and if the results are within normal limits, it is of great value; if the results are borderline or below normal it is almost useless. Normal pregnancy causes certain metabolic and physicochemical changes in the body which alter the excretion of water and solids by the kidney and thus affect renal functional tests.

Slemons, in 1904, noted in three normal pregnant patients that the average twenty-four-hour urine comprised 72, 53, and 48 per cent of the fluid taken by mouth, but that after delivery the urine volume increased to 81, 63, and 69 per cent, respectively, which he stated were essentially the average figures for men. In one patient with a dead fetus in utero the urine was 93 per cent before delivery and 85 per cent after delivery.

Holtermann, basing his opinion on the Kaufmann edema test,¹ stated that 25

¹One hundred and fifty cubic centimeters of water every hour from 7:00 A.M. to 1:00 P.M., and a comparison of the 8, 9, 10, and 11 A.M. specimens with those at 12 and 1, with the foot of the bed raised 25 cm. at 11 A.M.

per cent of all pregnant women without manifest edema showed latent edema. He did not regard this method as a test of heart function in pregnancy, but as a test of the capillary circulation, since he considered the edema of pregnancy to be due to increased permeability of the capillary walls.

Janney and Walker, using a water elimination test,² noted that in normal pregnancy the ability of the kidneys to excrete water steadily decreased, reaching a minimum of 67 per cent at thirty-six weeks. After delivery the urine volume steadily increased and by the ninth postpartum week it formed 92 per cent of the intake, without correction for the breast milk. In six toxemic patients the average output of urine was 17 per cent of the normal. In a subsequent report they demonstrated that the kidneys were far more efficient with the patient in the horizontal than in the vertical position, thus indicating the value of absolute bed rest not only in the toxemias of pregnancy, but in all patients with seriously impaired renal function.

We have repeated their work, and in a small series of 12 normal patients at term the percentage of urine was 36 per cent before and 78 per cent after delivery. Thus it is evident that there is a disturbance in the water excretion during pregnancy, and that any test which involves either the measurement of the volume of urine or the determination of the excretion of some substances for a given period will be decreased.

In Tables II, A and II, B are listed the means for the three-hour and one-hour volumes of urine (average of two one-hour periods) in normal and toxemic patients. The toxemic patients before delivery show this decreased water elimination or oliguria better than the normal patients who had not fasted for fifteen hours. Many patients did not secrete any urine between 9:00 A.M. and 10:00 A.M., and even at the end of the second period there would be only 10 or 20 c.c. These same patients after delivery, under identical conditions, would excrete 40 to 80 c.c. or more per hour, despite the extra need of water for lactation. In Table II, A, the difference before and after delivery in pre-eclampsia is of significance and emphasizes the oliguria which is characteristic of this disease. In Table II, B, the difference before and after delivery in Group III is of significance. In this group we thought that because of no previous history of toxemia the figures for the renal functional tests would be higher than in Group II. However, these patients had lower figures, indicating that the condition was either a different one or that the history was incorrect. They demonstrated the insidious onset of vascular-renal disease.

In Table II, C are listed the means for the specific gravity of the urine. While the difference between the antepartum and postpartum means in Groups I, II, and III is not significant, the data for each mean are obtained from the same patients; therefore, we believe that our figures do show the direction of change. The frequency of distribution, likewise, shows a preponderance of higher specific gravity

²All-night fast, intake of 200 c.c. of water every thirty minutes from 9:00 A.M. to 11:30 A.M., and a comparison of the volume of urine from 9:30 A.M. to 1:00 P.M., with the total intake of 1,200 c.c.

TABLE II

	NONCONVULSIVE TOXEMIA										ECLAMP- SIA	ABRUPTIO PLACENTAE
	NORMAL PREGNANCY		GROUP I		II		III					
			PREECLAMPSIA		HISTORY OF TOX- EMIA		NO HISTORY OF TOXEMIA					
			A.P.	P.P.	A.P.	P.P.	A.P.	P.P.	A.P.	P.P.		
<i>A. Volume of Three-Hour Urine in Cubic Centimeters</i>												
Total cases	18		14	25	35	25	17	12	26	25		
Mean	70.8		50.0*	115.5*	108.9	101.5	93.4	81.3	118.3	110.5		
Standard deviation	57.8		25.9	54.5	55.2	62.2	37.4	38.8	67.6	52.5		
Probable error	9.20		4.67	7.35	6.30	9.34	6.11	7.56	8.95	7.08		
<i>B. Volume of One-Hour Urine in Cubic Centimeters</i>												
Total cases	27	10	22	27	37	31	24	20	26	26		
Mean	55.1	47.5	36.4	54.2	45.6	66.5	38.5*	73.8*	65.3	73.1		
Standard deviation	46.9	31.7	23.2	40.3	37.7	62.1	24.5	57.9	54.0	53.0		
Probable error	6.09	6.75	3.34	5.23	4.18	7.50	3.37	8.73	7.15	7.01		
<i>C. Specific Gravity of Three-Hour Urine</i>												
Total cases	29	25	14	22	34	32	17	10	23	27		
Mean	1.022	1.029	1.016	1.019	1.019	1.020	1.018	1.019	1.016	1.018		
Standard deviation	0.0069	0.0071	0.0054	0.0076	0.0063	0.0074	0.0050	0.0057	0.0098	0.0079		
Probable error	0.0011	0.0012	0.0011	0.0012	0.0008	0.0011	0.0008	0.0012	0.0014	0.0010		

Means, standard deviations, and probable errors were derived from the usual frequency tables.

*Significant difference.

A. P. = Antepartum.

P. P. = Postpartum.

after delivery. The normal pregnant woman is able to excrete urine with an average specific gravity of only 1.022 after a fifteen-hour fast, probably because of the excess amount of water in her tissues (physiologic edema). With longer fast periods or after delivery or death of the fetus she is able to excrete urine with a specific gravity of 1.030 or even higher. The relatively low specific gravity in pregnancy is due to a decreased amount of solids, especially urea and chlorides. Data on urea are given in Table III, C, but since the specific gravity varies more with changes in electrolytes, any decrease in their concentration will lower the specific gravity. Normally, the kidney can concentrate NaCl to 1.3 per cent, but in many analyses in pregnancy we have seen only a few patients who could concentrate it to this degree. The range is from 0.01 to 0.9 per cent, with an average of 0.5 per cent. Large amounts of ingested chloride are excreted by an increase in the volume of urine. This low concentration of chloride in the urine, we believe, is due to changes caused by pregnancy in the permeability of the vessel and cell walls, which permit water and chloride to escape from the vascular system into the cell and interstitial spaces, but retard the return. The rapid disappearance of intradermal wheals of physiologic saline solution in pregnancy adds additional support to the opinion that the change is in the tissues and not in the kidneys.

The specimens of urine obtained on admission from 26 patients with eclampsia were always concentrated and highly colored, but contained an average concentration of NaCl of only 0.185 per cent (range 0.006 to 0.0550). In 12 patients with preeclampsia the average concentration of NaCl was 0.169 per cent (range 0.015 to 0.560). The urea nitrogen was also usually less than 500 mg. per cent. This low concentration of NaCl is probably extrarenal in origin because within a few hours the excretion of NaCl may be normal. In one patient with eclampsia three specimens of urine within the first twelve hours, with volumes of 12, 40, and 720 c.c., had a concentration of 0.21, 0.77, and 0.88 per cent, respectively. Thus if the specific gravity of the urine in pregnancy is 1.022 or more, there is no evidence of renal impairment, but if it is less, the determination is of comparatively little value.

The phenolsulphonaphthalein test was used in some 60 cases of severe toxemia. Only five patients with marked renal impairment excreted less than 50 per cent. Of course, in the eclamptic or preeclamptic patients with oliguria or anuria the excretion of the dye is diminished, but these same patients will have an excretion of 80 to 90 per cent of the dye as soon as the urine volume is normal, which has occurred in many cases both before and after delivery within twelve to twenty-four hours of the acute suppression of urine.

The MacLean urea concentration test was discarded because the comparatively low values of urine urea in both normal pregnant and

TABLE III

	NONCONVULSIVE TOXEMIA												ECLAMPSIA	P.P.	P.P.	P.P.	ABRUPTIO PLACENTAE				
	NORMAL PREGNANCY		GROUP I PRE- ECLAMPSIA		II HISTORY OF TOXEMIA		III NO HISTORY OF TOXEMIA		ECLAMPSIA		P.P.							P.P.		P.P.	
<i>A. Blood Nonprotein Nitrogen in Milligram Per Cent</i>																					
Total cases	14		27	27	39	28	23	20	30	21											
Mean	23.8		28.2	31.7	27.9	30.5	29.5	31.2	29.3	32.1											
Standard deviation	4.82		5.3	4.8	6.4	6.8	6.2	6.4	5.1	6.4											
Probable error	0.069		0.69	0.66	0.69	0.87	0.87	0.97	0.83	1.15											
<i>B. Blood Urea Nitrogen in Milligram Per Cent</i>																					
Total cases	28	10	26	30	39	33	24	23	26	26											
Mean	12.18	14.0	13.7	16.2	14.4	16.1	15.4	16.4	14.7	15.3											
Standard deviation	3.67	3.87	3.4	3.5	4.2	4.4	5.4	4.6	5.0	3.7											
Probable error	0.468	0.725	0.45	0.45	0.45	0.52	0.74	0.65	0.80	0.59											
<i>C. Urine Urea Nitrogen in Milligram Per Cent</i>																					
Mean	778.0	1001.0	479.0	632.0	588.0	654.0	452.0	700.0	508.0	540.0											

Means, standard deviations, and probable errors were derived from the usual frequency tables.

Means, standard deviations, and probable errors were derived from the usual frequency tables.

toxemic patients, even after urea by mouth, made the test of little value for diagnosis or prognosis.

The Addis technic for the microscopic examination of the urine was used in all cases, but was modified.* The Addis count is of the utmost importance in toxemic patients, but it is time-consuming if carried out according to the original technic, and we, therefore, suggest the modification.

In a previous publication we have given our results for the blood nonprotein nitrogen in the toxemias of pregnancy, but believe that the comparison of urea nitrogen and nonprotein nitrogen on the same patient is of importance. Therefore, in Tables III, A and III, B are listed the means for blood nonprotein nitrogen and urea nitrogen for the series reported in this paper. The difference between the means for the nonprotein nitrogen and the blood urea nitrogen before and after delivery was of no significance in all of the groups, but it should be noted that the means were always higher after delivery. Patients with a nonprotein nitrogen of 55 mg. per cent or blood urea nitrogen of 30 mg. per cent or more are not included in the statistical tables. These patients (relatively rare) are not representative of the vast majority of toxemic patients, and the inclusion of data from such cases would not give a proper conception of the toxemias of pregnancy. Thus in 2,252 analyses of the blood on approximately 600 toxemic patients, the nonprotein nitrogen was more than 50 mg. per cent in 21. In 342 blood urea determinations on 190 toxemic patients there were only 13 with more than 30 mg. per cent. As a rule, patients with renal impairment of sufficient severity to cause nitrogen retention do not conceive.

Since the introduction of the manometric determination of urea by Van Slyke, many extremely low figures for urea nitrogen have been reported. We have analyzed various standard solutions of urea and blood with Van Slyke's manometric, Leiboff's acid hydrolysis, and the xanthidrol methods, and if done carefully, with special emphasis on the proper clearing of the manometer (possible poisoning of the urease by the mercury salts), consistent results have been obtained. However, in the routine determination of blood urea in pregnancy by the manometric method in our laboratory and in two others, the figures in the majority of cases have been lower than those obtained by other methods. In a fair proportion of the cases the manometric data are undoubtedly incorrect. Thus Hurwitz and Ohler, in reporting their series of urea clearances in the toxemias of pregnancy, state that the average nonprotein nitrogen is 30, urea nitrogen 6.9, and uric acid

*The examination was made on a three-hour specimen obtained by catheterization after a fifteen-hour fast. No attempt was made to determine the total number of casts, epithelial cells, leucocytes, erythrocytes, etc., for twenty-four hours, but the average number of these various formed elements was determined in two low-power fields. If the number was small then eight fields were counted.

4.3. If these figures are correct the undetermined nitrogen is markedly increased. They report blood urea nitrogen of 2.8, 3.6, 4.5, 4.6, etc., with nonprotein nitrogen determinations on the same patients of 27, 25, 30, 20. In the group classed by them as chronic nephritis, the inconsistency is even greater.

The nonprotein nitrogen and blood urea nitrogen are diminished early in pregnancy and the decrease persists throughout. We have studied the same women throughout pregnancy and the puerperium and found that the average nonprotein nitrogen in the three trimesters was 25, 25, and 24 mg. per cent, respectively. In the first postpartum week it was 28, and in the second, 29 mg. per cent. We have no adequate explanation for the decrease in the nonprotein nitrogen or blood urea nitrogen. It is obviously not due to the passage of urea into the amniotic fluid because of its occurrence so early in pregnancy. However, we wish to point out that since the blood urea is the divisor in determining the U/B ratio, any lowering of it, whether real or artificial (error in method), will not only increase the U/B factor but also the clearance.

In Table IV are listed the means for the urea concentration factor. Rabinowitch stated that if 15 gm. of urea were given by mouth after an all-night fast, and blood and urine urea determined in one and two hours, the quotient derived by dividing the urine urea nitrogen by the blood urea nitrogen was an excellent indication of renal function. In normal individuals the mean was 47.3, with a standard deviation of 6.9. This factor forms part of the clearance equation, and since our clearances were obtained with restricted fluids, we have calculated the U/B ratio and believe it is of value. In normal pregnancy the range is from 9 to 119, mean 63.8, and the standard deviation is 32.6. This high figure is explained by the decrease in blood urea.

Since the Leiboff acid hydrolysis method with blood usually gives 1 or 2 mg. per cent more than the other methods, and the results with urine are essentially the same, then our figures for U/B and for the clearance should be slightly less than those based on other methods. However, to our surprise, in normal pregnancy, despite the tremendous range, the extremely high means of 63.8 before and 71.5 after delivery were found. With an average blood urea nitrogen of 6.9, as reported by Hurwitz, in contrast with our average of 12 mg. per cent, the urea concentration factor would be still higher. The means for Groups I, II, and III before delivery, despite the normal blood urea, are decidedly below the normal for pregnancy. This reduction is due entirely to the decrease in the concentration of the urine urea. We do not know whether this low concentration of urine urea before delivery is the result of renal damage, vascular spasm of the glomerular vessels causing decreased elimination, or of increased absorption of urea

in the tubules. In Group I the difference between the antepartum and postpartum means is of no significance. In Group III the difference is of significance and is especially low before delivery. It should be pointed out that most of our deaths have occurred in this group, in which there is no history of previous toxemia or cardiovascular renal disease. It should also be emphasized that despite the increase in the

TABLE IV. UREA CONCENTRATION FACTOR—VARIATIONS AND AVERAGE

U/B FACTOR	NORMAL PREGNANCY		NONCONVULSIVE TOXEMIA						ECLAMP- SIA	ABRUPTIO PLA- CENTAE
			GROUP I PRE- ECLAMPSIA		GROUP II HISTORY OF TOXEMIA		GROUP III NO HISTORY OF TOXEMIA			
	A.P.	P.P.	A.P.	P.P.	A.P.	P.P.	A.P.	P.P.	P.P.	P.P.
1- 9	1							3	1	4
10- 19	1		3	1	4	4	6		2	4
20- 29	2		6	5	8	4	6		7	8
30- 39	3	1	6	11	8	6	6	7	7	8
40- 49	4	3	7	7	5	8	2	5	5	1
50- 59	1		1	3	2	6		2	3	0
60- 69	1	1		1	4	2		1	1	1
70- 79	5	2	1		3			1		
80- 89	3			1	1	1	1	2		
90- 99	3									
100-109		1								
110-119	3	2								
Total	27	10	24	29	35	31	21	21	26	26
Mean	63.8	71.5	34.9	39.1	40.8	40.6	29.3*	42.6*	34.5	35.3
Standard deviation	32.6	29.8	13.6	14.9	20.4	16.9	16.3	22.0	14.0	13.6
Probable error	4.33	6.36	1.87	1.97	2.33	2.05	2.40	2.24	1.85	1.80

*Significant difference.

blood urea nitrogen, the U/B quotient is higher after than before delivery in Groups I and III. After eclampsia and abruptio placentae the quotient is slightly decreased, but not enough to indicate definite renal impairment.

In Table V are listed the variations and means for the Van Slyke urea clearance. All clearances are expressed as percentage of normal and are calculated as the standard, with but few exceptions. In the nonpregnant individual the standard clearance ranges from 40 to 68 c.c. (74 to 126 per cent), with an average of 54 c.c. (100 per cent) of blood, and the maximum clearance ranges from 65 to 103 c.c. (85 to 135 per cent), with an average of 76 c.c. (100 per cent) of blood. In 19 clearances on the author since 1930, the range has been from 43 to 170 per cent. On Dec. 11, 1933, and Feb. 8, 1934, hourly clearances with almost constant urine volumes were 130, 105, and 78 per cent, and 110, 120, 96, 128, and 115 per cent, respectively. However, it has been stated by all observers that one characteristic of the normal kidney is its marked variability in contrast with the impaired kidney

which shows constant low values. In normal pregnancy the mean is 102.3 per cent, with a standard deviation of 30.9. It is higher after delivery despite the increase in the blood urea, because both the urine urea concentration and the urine volume are increased.

TABLE V. UREA CLEARANCE, VARIATIONS AND AVERAGES

PER CENT	NORMAL PREGNANCY		NONCONVULSIVE TOXEMIA						ECLAMP-SIA	TIO ABRUP-PLA-CENTAE
			GROUP I PRE-ECLAMPSIA		GROUP II HISTORY OF TOXEMIA		GROUP III NO HISTORY OF TOXEMIA			
	A.P.	P.P.	A.P.	P.P.	A.P.	P.P.	A.P.	P.P.	P.P.	P.P.
10- 19					1		2	2	2	
20- 29			2	2	1		5	4	1	
30- 39			5	1	5	4	9		4	3
40- 49	1		4	1	8	6	1	5	3	3
50- 59	2	1	7	6	7	3	4	6	4	6
60- 69			4	8	3	5	2	1	3	9
70- 79	3		3	5	3	3	1	1	4	3
80- 89	5			2	4	3		2	3	1
90- 99	1	1			1	3		2	1	1
100-109	5	2		2	2			1	1	
110-119	2	2								
120-129	4					1				
130-139		1				3				
140-149	2									
150-159	1									
160-169										
170-179	1	3								
Total	27	10	25	27	35	31	24	24	26	26
Mean	102.3	124.5	50.5	63.2	57.4	64.5	38.7*	53.2*	57.2	56.4
Standard deviation	30.9	39.2	15.2	19.9	22.0	30.5	16.3	23.9	24.0	15.3
Probable error	4.01	8.36	2.05	2.74	2.51	3.69	2.24	3.29	3.18	2.02

*Significant difference.

In the nonconvulsive group, all of the clearances were greater after delivery than before, but Group III was the only one in which the increase was significant. Since the clearance before and after delivery was obtained on the same patient, it is evident that pregnancy does cause a decrease which, in Groups I and II, is due primarily to a diminished volume of urine per minute, but in Group III there is, in addition, a decreased concentration of urea. The means for the clearance in patients who had either eclampsia or abruptio placentae are 57.2 and 56.4 per cent, respectively. All of the means in the toxemic patients after delivery are less than 65 per cent.

In Groups I, II, and III, 44, 43 and 71 per cent, respectively, of the clearances are less than 50 per cent before delivery, and 15, 32, and 46 per cent after delivery. In the groups of patients in whom eclampsia or abruptio placentae occurred, 38 and 23 per cent, respectively, of the clearances are below 50 per cent.

Our purpose in using the clearance test was to determine its value in pregnancy as an aid in differential diagnosis and prognosis. One difficulty encountered in properly interpreting its values is that the range for the normal nonpregnant individual is still too great because of the relatively few observations that have been made. It is obvious that the urea clearance is of little value in pregnancy in the majority of cases as an aid in diagnosis or prognosis. After delivery it is of value in determining if the kidney function has returned to normal, but it does not aid very much in determining whether or not the patient has nephritis. If the clearances are all low and there is no marked pathology of the cardiovascular system, it then indicates that the amount of functioning kidney tissue is decreased.

COMMENT

Spalding, Shevky and Addis, in 1922, stated that their results suggested the possibility of an increase in the amount of effective kidney substance during pregnancy, and that the decrease in the ability of the kidneys to excrete urea in toxemic patients was a real decrease and was not due to the pregnancy itself. In three patients with marked renal impairment, they suggested that the chronic kidney lesion might have had its origin in an unhealed nephrosis contracted during a toxemia of pregnancy. They also noted, especially in toxic patients, a tendency toward an oliguria. They concluded that, provisionally, the renal lesion in the toxemia of pregnancy was important not before, but after, delivery.

Hurwitz and Ohler reported clearances in 21 toxemic patients and stated that in 13 the clearance was normal and in 8 it was less than normal. The average was 111 per cent. In 17 patients with chronic nephritis they found three with normal and 14 with low clearances. The average was 64 per cent. The average clearance in five patients after eclampsia was 61 per cent. In five normal pregnant patients the average clearance was 127 per cent. They concluded that the urea clearance checked up well with the clinical diagnosis, in that it was normal in the toxemias, decreased in the acute stage of eclampsia, and low with a high degree of consistency in chronic nephritis. They also stated that their data suggest a correlation between the unusually high urea clearance and the low blood urea nitrogen in normal pregnancy. The comparatively high figures for the clearance may be due to the low blood urea nitrogen, for which their average was 6.9 in the toxemic, and 9.8 mg. per cent in the nephritic, group.

Cantarow and Ricchiuti, in a study of the urea clearance in pregnancy, stated that in 39 normal pregnant women, the urea clearance values ranged from 28 to 184 per cent; the average was 71.5 per cent (54 c.c. = 100 per cent). The urea clearance which was normal early in pregnancy diminished as pregnancy progressed, being rather consistently low a few days before the onset of labor. Subnormal clearance values obtained during the last two months of gestation must be interpreted with extreme caution, particularly in the absence of clinical or laboratory evidence of renal dysfunction.

Stander and coworkers, in 1932, used various renal functional tests in the toxemias and concluded that the urea clearance, guanidine and creatinine excretion tests were of real value in the differentiation between mild nephritis and the other toxemias of pregnancy. They stated that a urea clearance below 80 per cent is strongly indicative of renal damage. Since the first publication, Stander has become more cautious in interpreting the urea clearance, and in a recent report states as follows: "Any urea clearance which gives values below 50 per cent is very strong proof of the existence of a chronic nephritis. A urea clearance above 50 per cent does not necessarily mean that the patient does not have chronic nephritis, and in these cases it is necessary to study the patient further."

The fact that the various renal functional tests do not show marked kidney impairment after the toxemias of pregnancy does not mean that they should be discarded. The diagnosis of preeclampsia or eclampsia, primary or secondary hypertension, nephrosis, acute or chronic glomerulonephritis should be based on the history, physical examination and *repeated* examinations of blood, urine, and kidney function. Thus a patient with a persistent hypertension after delivery, but with normal or low normal renal function, would be diagnosed as having primary hypertension or hyperpiesia. However, we believe that pregnancy can be the etiologic agent in causing the hypertension and, if so, the diagnosis then would be secondary hypertension. This point requires further investigation. Similarly, the patient in whom the urea clearance is (1) persistently below 50 per cent; (2) the maximum specific gravity of the urine is 1.015 or less; (3) the Addis count reveals an abnormal increase in formed elements, or (4) any standard renal functional test showing a significant decrease, would be diagnosed as having renal impairment. This condition might have as its etiology an acute glomerulonephritis, a primary hypertension, with renal impairment due to nephrosclerosis, a pyelitis and hydro-nephrosis with destruction of kidney substance, a preeclampsia or eclampsia, or an abruptio placentae. Only by careful observations and repeated blood and urine studies in these toxemic patients over a period of years can the various diseases be satisfactorily explained and classified.

CONCLUSIONS

In Normal Pregnancy.—

1. The means for the blood nonprotein nitrogen and urea nitrogen which are 23.8 and 12.2 mg. per cent, respectively, are below normal.
2. There is a delayed or decreased elimination of water by the kidney.
3. The concentration of urea and NaCl in the urine is decreased and, therefore, the mean for the maximum specific gravity of the urine is 1.022.
4. The mean for the urea concentration factor is 63.8 before and 71.5 per cent after delivery. This increase above the normal is caused by the reduction in the blood urea.

5. The mean for the urea clearance is 102.3 before and 124.5 per cent after delivery.

6. The urea clearance, despite the decrease in the blood urea, is apparently decreased in the last half of pregnancy, if studied in individual patients.

In the Toxemias of Pregnancy.—

1. The averages for the blood nonprotein nitrogen and urea nitrogen are 30.6 and 14.5 mg. per cent, respectively. In the absence of a hypochloremia or an oliguria, a nonprotein nitrogen of 40 mg. per cent or more, or a urea nitrogen of 20 mg. per cent or more, should always suggest renal impairment. Patients with sufficient kidney pathology to cause a nitrogen retention as a rule either do not conceive or if they do, death of the fetus or mother usually occurs early in the pregnancy.

2. The urinary excretion of water is even more markedly decreased than in normal pregnancy. This delayed or retarded water elimination may be due to an arteriolar spasm of the renal vessels, thus diminishing the glomerular filtrate, or to increased reabsorption of water in the tubules. Lack of water in the blood stream (hemoconcentration), because of the increased permeability of capillary and cell walls due to the toxemia, may also be a factor.

3. The concentration of urea and NaCl in the urine is still further decreased, thus resulting in an average specific gravity of 1.018 before and 1.020 after delivery.

4. The mean for the urea concentration factor is slightly less than that given for the nonpregnant individual. It is approximately one-half of the mean for the normal pregnant patient.

5. The urea clearance test in patients with toxemia, hypertension, or nephritis, as a rule, is definitely decreased during the latter half of pregnancy. This impairment is caused by the reduction or delay in the elimination of water and the diminished concentration of urea in the urine.

6. A urea clearance after delivery, which is persistently 50 per cent of the normal or less, indicates renal impairment. This organic renal change may be the result of preeclampsia, eclampsia, nephrosclerosis, glomerulonephritis, or of pyelonephritis.

7. Many patients, over a period of three to six months after delivery, show considerable increases in the clearance. The phenomenon may be explained by assuming an hypertrophy of the remaining kidney tissue, or a slowly decreasing arteriolar spasm of the renal vessels, thus permitting more filtration. Therefore, renal functional tests for diagnostic value should be performed weeks, or preferably months, after delivery.

8. The Addis count is of considerable value in differentiating the various types of toxemia during pregnancy.

9. Careful observations and *repeated* studies of the blood, urine, and renal function over a period of years in a large number of toxemic patients are essential for a proper classification.

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Khreninger-Guggenberger and Leutenmayer: Primiparae in the Fifth Decade of Life, Arch. f. Gynäk. 154: 309, 1933.

The incidence of primiparas more than forty years old has increased in Germany since the World War. The authors report on 151 such patients delivered in the Munich Frauenklinik. They found among them a higher incidence of contracted pelvis with a correspondingly high morbidity and mortality. Another serious complication in this group is the high rate of cardiac disease; there was no increased incidence of renal disease; eclampsia was not encountered. Apparently the percentage of women carrying to term decreases as the age increases since one out of every six in this group had a premature labor.

The duration of labor during the fifth decade is no greater than in the fourth decade; labor lasted longer than twenty-four hours in one out of four, and longer than two days in one out of every 27. Premature rupture of the membranes occurred once in every 3.5 patients. Every third labor was terminated by operative delivery; one in six by forceps.

The fetal mortality is high, there being one death in every 5.5 deliveries.

RALPH A. REIS.

Macchiarulo, O.: A Case of Primary Echinococous Cyst Infestation of the Uterus, Folia gynec. 31: 89, 1934.

After a review of the few cases of echinococous cyst infestation of the uterus reported in literature, the author describes a case of primary infestation of the uterus observed by him. He concludes that the only rational treatment is hysterectomy.

MARIO A. CASTALLO.

A CLINICAL COMPARISON OF VARIOUS ERGOT PREPARATIONS ON THE POSTPARTUM HUMAN UTERUS

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CONSIDERABLE experimental work has been done on the effects of various extracts as well as of a number of pure drug principles derived from the fungus ergot on the uterus of animals both in vitro and in situ. However, comparatively few controlled observations have been made on the gravid or postpartum human uterus in situ. The published reports of these observations are somewhat conflicting, due probably to the different methods of study which have been used.

The modern study of ergot began in 1906 when Barger and Dale¹ isolated an alkaloid in pure crystalline form which they called ergotoxine. Previous to this time, however, because of impure chemical preparations, no active principle of ergot had been isolated. Ergotoxine was found to be highly active, and, under experimental conditions, produced all the typical pharmacologic actions of ergot. It also proved to be closely related to Tanret's ergotinine isolated in 1875 but found to be inert. Ergotoxine, prepared by the Burroughs Wellcome and Company, was considered the specific alkaloid and most active principle of ergot until 1921 when Stoll of the Sandoz Laboratories isolated ergotamine which he claimed to be a crystalline compound of slightly different composition than ergotoxine. The correspondence between Stoll and Dale in which the problem of recognition of their respective products as the specific alkaloid of ergot was discussed, appeared in *Lancet*² in 1930. More recently, others³ have published work indicating that ergotoxine and ergotamine are equivalent as to pharmacologic action although slightly different chemically. Moir⁴ observed no clinical differences between these products. During the last year, two entirely new alkaloids of ergot have been isolated by American drug firms and made available for clinical trial. We feel that the state of our knowledge of the clinical effectiveness of the various ergot preparations is still incomplete, particularly from the standpoint of quantitative reactions, as well as the relative duration of action on the postpartum uterus.

The U.S.P. fluid extract of ergot is generally considered to be the most reliable of the series of drugs available for limitation of postpartum hemorrhage and acceleration of involution of the uterus. However, the B.P. liquid extract continues to be used in England although some⁵ have cast doubt on the efficiency of this preparation in that it was reported to be devoid of alkaloids. Carr and Dale⁶ criticized the methods used for preparing the liquid extract in that ergotoxine was thus eliminated. Bourne and Burn⁵ concluded that the B.P. liquid extract was clinically inert due to the small amount of alkaloids present. These authors compared the effectiveness of different ergot preparations by observing the rate of uterine involution during the postpartum period. Moir,⁷ however, studied the reaction of the postpartum uterus to a series of ergot preparations (using the bag induction technic) and found the reactions to the B. P. liquid extract of ergot to be more rapid and of greater magni-

tude than that obtained with any drug previously used. This reaction was ascribed to an unknown active principle in that he considered his liquid extracts as being alkaloid-free; thus the oxytocic reaction could not be due to ergotoxine, ergotinine, histamine, or tyramine.

The present study was undertaken in order to clarify the conflicting reports as to the relative clinical efficiency of the B.P. liquid and the U.S.P. fluid extracts of ergot. It has been supplemented by a comparison of the reaction of the postpartum uterus to ergotoxine, gynergen, ergot aseptic, histamine, tyramine, pituitrin, and morphine.

METHODS

Two methods have been utilized for the study of the postpartum human uterus in situ, i.e., the insertion of a bag into the uterus and recording uterine motility by changes in hydrostatic pressure as described by Bourne and Burn,⁵ Moir,⁷ Adair and Davis,⁸ and the indirect or abdominal tambour method first used by Rubsamén⁹ in 1913.

The hydrostatic bag method has certain advantages in that very fine movements of the uterus are recordable, which might be insufficient in degree to be indicated by the indirect records of uterine movements as obtained from the abdomen. Further, the position of the uterus would not significantly alter the type of record obtained directly, whereas changes of position of the uterus are of significant importance when motility is observed by the indirect method. On the other hand, the uterus reacts to the presence of the bag as to a foreign object, and the motility due to the distensive stimulus probably is of abnormal type. The use is limited to the sixth or seventh postpartum day or after low cervical cesarean section, and is attended by the danger of infection.

The method used in the present report is that described by Dodek¹⁰ with the exception of a minor modification of the abdominal tambour. The apparatus consisted of a delicate abdominal tambour which was supported in an upright position by a metal tripod strapped firmly to the patient's abdomen by means of adhesive tape. This tambour was placed so that the button at the end of the recording lever firmly contacted the abdominal wall directly over the dome of the uterine fundus. Movements of the uterus were transmitted by air pressure from the abdomen to a second tambour, the excursions of which were recorded in ink on a clock-driven paper. This method may be used during the course of labor or repeatedly at any convenient time during the postpartum period. Patients were not subjected to pain or discomfort during the course of a record of uterine movements, but were required to remain quiet with minimal muscular movements for approximately two hours. The limitations of this procedure necessitate choosing patients with moderate to thin abdominal walls for optimal records. Patients were encouraged to void urine before beginning a tracing, as a full or rapidly filling bladder predisposed to restlessness, and, in addition, tended to alter the position of the uterus with resulting errors in the graphic records. For the same reason, the routine castor oil, as administered in this hospital, was not given if uterine tracings were to be made on the first postpartum day. The reactions to various medicinal agents as observed by the indirect method compare very closely with those obtained by the bag induction method. The indirect method, therefore, appears to offer a safe and reliable clinical assay procedure for various oxytocic agents useful during the third stage of labor or the postpartum period. In addition, the type of uterine activity is helpful in judging the rate of involution.

RESULTS

Uterine movements are most active shortly after delivery, but quite regular optimal reactions are obtainable by the indirect method used during the first four postpartum days. Our data were obtained from

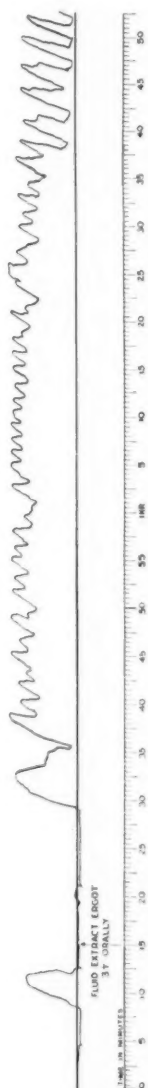


Fig. 1.



Fig. 2.

one hour after delivery to the fourth postpartum day, but, as a rule, records were obtained on the first or second postpartum day because of greater convenience. At this time, patients have completely recovered from any premedication sequence or anesthesia and are more comfortable and cooperative.

The routine of an experiment was as follows: a control tracing of the uterine movements was obtained over a forty-five-minute period, after which the drug selected for testing was administered and continuous tracings obtained during the subsequent sixty to ninety min-

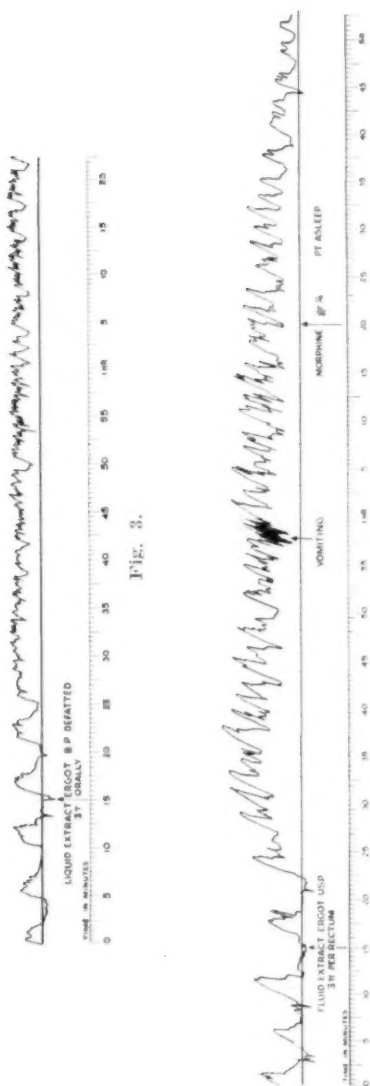


Fig. 3.

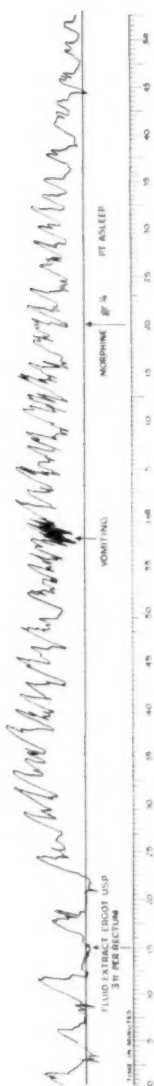


Fig. 4.

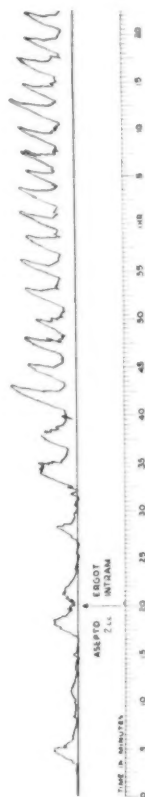


Fig. 5.

utes. The duration of action of certain of the agents tested was checked by later tracings on the same patient.

The uterine responses of individual patients were of the same order in that rhythmicity and contractility were maximal shortly after delivery and gradually diminished with time after delivery. However, the recorded responses of different patients varied widely so that ac-

accurate measurements of the responses for purposes of comparison appeared impractical. The time of reaction was recorded accurately but changes in frequency, contractility, and tone were tabulated as plus, minus, or no change. The percentile frequency of these reactions has been used for illustration. More detailed differences will be discussed in the text.

The reaction of the uterus to ergot administered by different routes is indicated in Table I. This illustrates the time and frequency of reaction to the U.S.P. fluid extract and the B.P. liquid extract administered orally, Parke, Davis and Co. ergot aseptic intramuscularly, and to the U.S.P. fluid extract rectally.

TABLE I

METHOD	DRUG	DOSAGE (C.C.)	REACTION TIME (MINUTES)		PER CENT SHOWING INCREASES			EFFI- CIENCY* HIGH (1) TO LOW (4)
			MIN.	MAX.	FR.	HT.	TONE	
Oral	U. S. P.	4	12.0	25.0	100	70	90	2
Oral	B. P.	8	11.5	25.0	100	100	100	3
Intramuscu- larly	P. D. & Co. aseptic	2	9.5	25.0	100	50	100	4
Rectal	U. S. P.	8	7.5	22.5	100	100	100	1

*Estimated by the degree and duration as well as by the frequency of stimulation.

The uterine response to preparations of ergot is somewhat more erratic after oral than after intramuscular injection of ergot aseptic or the rectal instillation of the U.S.P. fluid extract due to differences in the rate of absorption and occasional nausea and emesis. The rectal administration of the fluid extract (diluted with two to three volumes of water) offers certain advantages in that the injection may be made immediately after delivery, nausea or emesis is not encountered, and the uterine stimulation occurs more promptly and is greater in degree than after oral or intramuscular injections of ergot. Ergot aseptic was next most regular as to the uterine responses obtained. The intramuscular injection offers certain advantages in that medication can be given immediately after completion of the third stage of labor. However, the degree of response was distinctly less than in the case of either the fluid or liquid extracts on oral administration. The observed differences are quite probably due to the minimal dosage of the aseptic injected, but the danger of infection is present and conscious patients complain of pain. The psychic reaction to the pain of such injections is reflected by a significant depression of uterine motility for ten to twenty minutes.

The dosages of the ergot preparations used varied from 2 to 8 c.c. A maximum dose of the fluid extract (4 c.c.) produced such disagreeable uterine cramps that in later observations 2 c.c. dosages were used.

The reactions obtained from this minimal dose were grossly comparable to those obtained with a 4 c.c. or drachm dose of the liquid extract.

The uterine reaction to small or medium dosages of ergot is reflected by an increased frequency and height of contraction with a moderate increase in tone. With maximal dosages, a spastic or tonic reaction occurs in that the tone rises maximally, and the uterus remains firmly contracted for twenty-five to forty-five minutes. The latter type of contraction is quite painful and patients become restless and complain. The two reactions are the same and differ only quantitatively and are modified partly by the irritability of the uterus but primarily by the dosage administered.

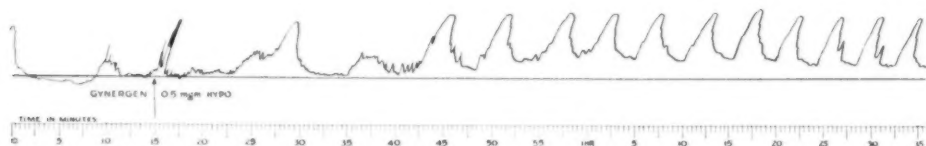


Fig. 6.

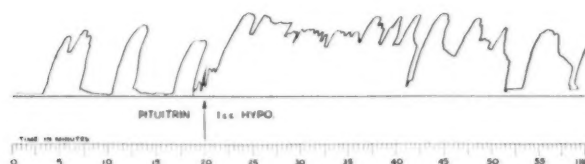


Fig. 7.

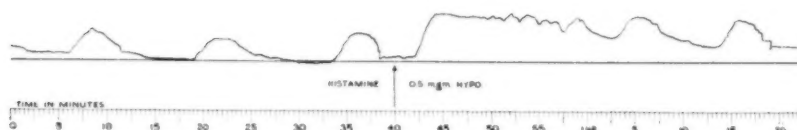


Fig. 8.

The influence of age on the rate of deterioration of both the U.S.P. fluid extract and the B.P. liquid extract was observed by making clinical tests of the potency of standard dosages of the preparations obtained from the same stock of crude ergot over a period of twelve months.

The U.S.P. fluid extract and the B.P. liquid extract (defatted and not defatted) were prepared and assayed chemically by Mr. E. D. Davy of the School of Pharmacy from a high grade Spanish (rye) ergot obtained through the courtesy of Dr. E. H. Volwiler of the Abbott Laboratories. A sufficient supply of these preparations was made to permit correlation of the clinical tests and the alkaloidal content of the extracts over a twelve-month period. In addition, the clinical effectiveness of the alkaloids (diluted to comparable volumes) obtained

from both the U.S.P. and B.P. extracts was compared with that observed with the alkaloid-free extracts.

The ergot preparations were made in November, 1932, and assayed in December, 1932, by the colorimetric method of M. I. Smith. The alkaloid content as compared with a standard ergotamine ethanesulphonate solution at that time is as follows:

Fluid extract of ergot U. S. P.	5.38 mg. alkaloids per 10 c.c.
Liquid extract of ergot B. P. (not defatted)	1.60 mg. alkaloids per 10 c.c.
Liquid extract of ergot B. P. (defatted)	1.44 mg. alkaloids per 10 c.c.

The relative clinical effectiveness of the U.S.P. fluid extract and the B.P. liquid extract over a period of one year together with the

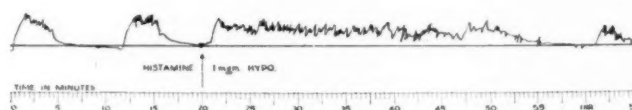


Fig. 9.

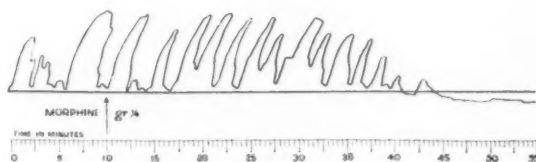


Fig. 10.

chemical assay of the alkaloids contained is illustrated in Table II. Deterioration according to the chemical assay method was very rapid and was complete so far as the limits of the colorimetric methods indicated within one year, at which time the preparations were stimulant to the uterus although the potency was reduced at least 75 per cent. The reaction of the uterus to the aged preparations was greatly

TABLE II

DATE	DRUG	(MG.) ALKALOIDS IN 10 C.C.	REACTION TIME (MINUTES)		PER CENT SHOWING INCREASES		
			MIN.	MAX.	FR.	HT.	TONE
Dec., 1932	U. S. P. fluid extract (E. D. Davy)	5.38	12	25	100	70	90
June, 1933	U. S. P. fluid extract (M. I. Smith)	0.75	27	35	100	0	0
Nov., 1933	U. S. P. fluid extract (E. D. Davy)	0.00	47	70	100	100	0
Dec., 1932	B. P. liquid extract* (E. D. Davy)	1.60	11.5	25	100	100	100
June, 1933	B. P. liquid extract (M. I. Smith)	0.30	55.0	78	100	100	0
Nov., 1933	B. P. liquid extract (E. D. Davy)	0.00	42.5	70	100	0	0

*The liquid extract was not defatted.

delayed as to the time of development and was limited to an increase in frequency with a slight increase in the amplitude of contraction. No increase in tonus was observed.

We are unable to explain the discrepancy between the observed clinical effectiveness of the aged ergot preparations and the theoretical potency as indicated by the absence of alkaloids. Samples of the official U.S.P. and B.P. preparations were sent to Dr. M. I. Smith of the U. S. Public Health Department in May, 1933. The possible upper limits of their alkaloidal contents as observed by Dr. Smith are indicated in the table. He reported that the preparations should be clinically inert. It is imaginable that the active principles, if due entirely to alkaloids, may have become altered in some manner during deterioration, so that although some activity remained, the principles were not detectable by the chemical assay method.

IS THE OXYTOCIC ACTIVITY OF ERGOT DUE TO ALKALOIDS ALONE?

Bourne and Burn compared the efficiency of a series of ergot preparations by noting the influence of these agents on the rate of uterine involution (as judged by the height of the fundus above the pubis) during the postpartum period. The B.P. liquid extract was considered inert. Moir observed the uterine responses (by the bag induction method) to both the U.S.P. and B.P. extracts as well as to other oxytocic principles, and concluded that the reactions to the B.P. liquid extract were more rapid in development and of greater amplitude than the responses to any other agent tested. This activity was ascribed to a new hypothetical principle (nonalkaloidal in character) and not attributable to histamine. His analysis of the liquid extract indicated that it was alkaloid-free.

The clinical efficiency of our U.S.P. and B.P. extracts together with the reactions to the alkaloids (from the B.P. extract) alone and the alkaloid-free B.P. extract is illustrated in Table III.

The alkaloids were removed from the liquid extract with ether in an automatic extractor, after evaporating the alcohol and rendering

TABLE III

DRUG	DOSE (C.C.)	ALK. PER 10 C.C. (MG.)	REACTION TIME (MINUTES)		PER CENT SHOWING INCREASES		
			MIN.	MAX.	FR.	HT.	TONE
(1) Fluid extract ergot U. S. P.	4	5.38	12.0	25	100	70	90
(2) Liquid extract ergot B. P. d.f.*	8	1.44	13.0	20	100	84	100
(3) Liquid extract ergot B. P. n.d.f.*	8	1.60	11.5	25	100	100	100
(4) Pure alkaloid soln. from No. 3	8	1.60	20.0	28	100	66	66
(5) Alkaloid-free soln. from No. 3	8	0.00	26.0	35	60	40	0

*d.f., defatted; n.d.f., not defatted.

the residue alkaline with ammonia. Extraction was continued for four hours, after which a negative test for alkaloids was obtained. The residue was acidified slightly with hydrochloric acid, the ether dispelled and the product diluted with alcohol to the original volume of the liquid extract. The same procedure was followed in handling the alkaloids represented in the ether extractive.

Table III illustrates the median results from a series of 30 patients who had been given the various ergot preparations by mouth. The B.P. nondefatted liquid extract appeared somewhat more efficient than the defatted extract. The difference in alkaloid content is not very great but probably enough to account for the differences in stimulation. On a dose basis, the B.P. ergots appeared about one-half as active as the U.S.P. fluid extract. One important difference observed was the lower frequency of spastic (painful) uterine reactions to the liquid extract. However, the activity of this preparation was greater than might be expected on the basis of its alkaloid content, in that the U.S.P. fluid extract on the same basis should be approximately three times as active as the B.P. extract. This discrepancy might be explained in several ways. First, the uterus probably reacts maximally to a given dose of alkaloid, and any more than this quantity has no further effect. We assume that our dosages were maximal in most patients studied. This is again emphasized by the fact that after the uterus had reacted to a maximal dose of ergot, the administration of a second dose within two to two and a half hours after the first dose was not followed by a significant further stimulation. Blair-Bell¹⁵ in his studies on pituitrin observed that the initial injection produced marked uterine contractions and a rise in tone; but, as with a second dose of ergot, subsequent injections of pituitrin produced minimal or no reactions unless a certain interval of time (one to two hours) was allowed to elapse between the first and second doses. The state of irritability of the uterus and, particularly the nature and time of previous medication is of significant importance so far as clinical assays are concerned.

A second possibility is that the standard assay methods (chemical and biologic) do not give a wholly satisfactory index of the clinical efficiency of the ergot preparations. Comparison of the stimulant properties of the total alkaloids from either of the official pharmacopeial preparations with that of the original products indicated the greater potency (35 per cent) of the original extracts. However, the original extracts rendered alkaloid-free according to chemical tests by extraction of these principles continued to produce a slight stimulation of the uterus. No explanation is offered as to why the original extracts were of greater potency than the alkaloids contained in them, or that the alkaloid-free extracts retained a slight activity. Our observations do not confirm those of Bourne and Burn in that the B.P.

liquid extract is not inert clinically although its efficiency is probably less than half that of the U.S.P. fluid extract. On the other hand, we cannot agree with Moir either as to the outstanding high efficiency of the B.P. preparation or the nature of the active principles. There is no reason for doubt that quite significant amounts of alkaloids are extracted by the B.P. method, due to the presence of plant acids in the crude drugs. Observations indicate that the oxytocic activity of ergot extracts is primarily due to alkaloids which are detectable clinically.

THE INFLUENCE OF PURE DRUG PRINCIPLES ON UTERINE ACTIVITY

The influence of gynergen, ergotoxine, histamine, tyramine and pituitrin on the postpartum uterus is indicated in Table IV. Gynergen,

TABLE IV

DRUG	DOSE (MG.)	REACTION TIME (MINUTES)		PER CENT SHOWING INCREASES			DURATION (HOURS)
		MIN.	MAX.	FR.	HT.	TONE	
Ergotamine tartrate (gynergen)	0.5	21.0	50	82	46	55	1.5-2.0
Ergotoxine ethanesul- phonate	0.5	29.0	51	51	100	0	1.5-2.0
Histamine acid phos- phate	0.5	1.5	1.5	100	100	100	0.5-0.75
Tyramine acid phos- phate	40.0	19.0	30	0	100	0	0.5-0.75
Pituitrin	1.0 c.c.	4.7	4.7	100	100	100	0.75-1.5

or ergotamine tartrate, was administered to fifteen patients usually subcutaneously but also orally and intramuscularly. The stimulant effects develop within fifteen to twenty-five minutes after injection, gradually increase in degree and become maximal by the fiftieth minute. The reactions are rather variable and less dependable than with either Galenic preparation studied. The rate of absorption (subcutaneous or intramuscular injection) judged by the time at which initial and maximal stimulation of the uterus appears is distinctly less than with the liquid or fluid extract administered orally. The reactions differed only quantitatively (outside of the time factors) from those of the extracts and could be explained theoretically on a basis of the difference of the alkaloid dosage administered, in that the gynergen dosage administered was only slightly more than one-third that present in the extracts. However, the injection of a milligram dose of gynergen produced distressing symptoms (headache, nausea, and vomiting) without any significant improvement of the uterine reactions seen with smaller doses. Oral dosages of gynergen of 1.0 mg. were ineffective.

Broom and Clark¹¹ (1923) reported that ergotoxine was approximately one-half as active biologically as ergotamine. Burn and Ellis¹² (1927) found the two

alkaloids equally active. Pattee and Nelson¹³ (1929) using the same test method as Broom and Clark, observed that ergotoxine was 33 per cent more active than ergotamine. In a more recent publication, Lozinski, Holden and Diver¹⁴ (1934) compared the efficiency of a series of ergot preparations by parallel colorimetric determinations of the alkaloid content and biologic activity. These authors concluded that ergotoxine was 66 per cent more active than ergotamine although the color reaction of ergotamine was distinctly greater than that of ergotoxine. Thus, if an extract contained ergotamine as the preponderant alkaloid, the biologic activity should be less than indicated on the basis of the colorimetric tests, but if ergotoxine was present in preponderance, the reverse might well be true.

A possible explanation of the contradictory reports relative to the biologic activity of the two ergot alkaloids may be given from our results. Our first tests of ergotoxine acid phosphate on the human uterus indicated practically no activity. Dr. C. S. Leonard of the Burroughs Wellcome and Company stated that this preparation had quite probably deteriorated. Subsequent tests of a new supply of ergotoxine ethanesulphonate of known potency indicated that ergotoxine was at least as stimulant to the human uterus as ergotamine.

Ergotoxine ethanesulphonate compared favorably with gynergen as to the rate of absorption, degree, and type of the reaction. This was usually limited to an increase in frequency with little or no changes in the height of contractions or tonus.

Tyramine administered hypodermically in maximum therapeutic dosages was of little value in that the stimulant effects were of negligible importance and restricted primarily to a small increase in the contraction heights. This type of reaction confirms similar observations of earlier reports.

The oxytocic effect of ergot administered orally is not dependent on any histamine contained, in that this substance is rapidly destroyed, and effective oral dosages of histamine per se are of the order of 8 mg. However, when administered subcutaneously, histamine produces a very prompt stimulation of all smooth muscle structures, including the uterus, in addition to the marked acceleration of secretions as utilized for gastric secretory tests. Dosages of 0.5 mg. rendered the uterus tonic within one and a half minutes after hypodermic injection. The tone gradually decreased from this peak with increasing amplitude and frequency of individual contractions but returned to normal after thirty-five minutes. With dosages of one milligram, the tonic uterine response was exaggerated but the development of undesirable side actions (marked vasodilatation, bronchial spasm, and accelerated pulse rate) indicated that this dosage was excessive.

Pituitrin affected the uterus in the same direction as histamine. Absorption was quite rapid, i.e., approximately twice as rapid as with extracts of ergot orally or rectally, and duplicated the effects of maximal dosages of ergot. With optimal dosages, the uterus became tonic for thirty to thirty-five minutes. This tonicity was followed by

an increase in frequency and height of the individual contractions over the control curve. Stimulant effects persisted for approximately 1.5 hours.

The influence of therapeutic dosages of morphine on the postpartum uterus was noted in a group of patients previously medicated with maximal dosages of ergot. This narcotic was administered in $\frac{1}{4}$ grain dosages subcutaneously to relieve the discomfort due to marked tonic uterine contractions. Such dosages promptly relieved the patients, but, in addition, the uterine tone decreased gradually to normal within twenty to thirty minutes, and in several cases motility and tone became definitely subnormal, and this was accompanied by an increased uterine blood loss. These data indicate the important relationship which exists between impulses from the central nervous system and uterine motility, and suggest that morphine should be administered cautiously during the early postpartum period because of the possible loss of uterine tone with a resultant increase in the postpartum hemorrhage.

SUMMARY AND CONCLUSIONS

1. The clinical efficiency of extracts of ergot as judged by the reaction of the postpartum uterus differs significantly according to the mode of administration; so far as the speed of reaction is concerned, the order is rectal, intramuscular, and then oral. However, the maximal differences in point of time ranged from 7.5 to 12 minutes with the three routes of administration. The order of magnitude and duration of response has the following order from the greatest to the least: rectal, oral U.S.P. fluid extract, oral B.P. liquid extract, and ergot aseptic intramuscularly. The difference of reaction efficiency between intramuscular and oral routes of administration is possibly a matter of dosage. The intramuscular injection may be given at any time during the postpartum period and nausea and vomiting do not occur, but the chance of infection is always present and the patient is subjected to pain. The rectal administration of the fluid extract (diluted with 2 to 3 volumes of water) produces optimal reactions and has the same advantages of intramuscular injections, and none of the disadvantages of either oral or intramuscular injection. The rectal administration appears to be the route of choice.

The maximal effects of the crude drug principles persist for forty-five to ninety minutes, and stimulation is still apparent up to four hours after oral or rectal administration. Responses to second dosages within two hours are negligible. The dosage frequency should not exceed every three to four hours.

2. The B.P. liquid extract of ergot is approximately one-half as effective as the U.S.P. fluid extract. The rate of absorption on oral administration is almost exactly the same as for the U.S.P. preparation. The B.P. liquid extract contains significant quantities of alka-

loids but slightly less than one-third of the quantity present in the U.S.P. fluid extract made from the same crude ergot. The activity of both preparations is primarily, but not entirely, dependent on the alkaloidal content of the extracts as indicated by the chemical methods of assay.

3. Aging of the U.S.P. fluid extract results in a deterioration of approximately 85 per cent on the basis of chemical tests for alkaloids in a period of eight months, although the clinical efficiency decreased not more than 50 per cent during the same period of time. The alkaloidal tests of either the U.S.P. or B.P. extracts after one year were negative. Nevertheless, these alkaloid-free solutions retained a clinical activity equivalent to 15 to 25 per cent of the original potency. The B.P. extracts deteriorated at approximately the same rate as the U.S.P. preparation of ergot (alkaloidal basis) and likewise exhibited a slight clinical activity at the end of one year. We are unable to explain the discrepancy between the chemical tests for alkaloids and the observed clinical tests after twelve to fourteen months' aging. There is a possibility that the active principles may have been altered in some manner during the deterioration, so that they were not detectable by the chemical assay methods used.

4. Ergotamine tartrate (gynergen) and ergotoxine ethanesulphonate produce changes in the postpartum uterus of the same character and order of magnitude. These principles administered hypodermically or intramuscularly are absorbed more slowly, and in dosages free of undesirable side actions (nausea, emesis, etc.), are distinctly less effective than the crude drugs administered by rectal, oral, or intramuscular routes.

Histamine in a dosage of 0.5 mg. hypodermically produces a tonic contraction of the uterus within one to two minutes. The spastic reaction diminishes gradually and disappears within thirty to thirty-five minutes after the injection. Larger doses, because of undesirable circulatory and general smooth muscle reactions, do not appear advisable. When the relatively negligible differences in speed of reaction and more particularly the duration of action are considered, the crude drug principles are to be preferred.

The administration of tyramine in maximal therapeutic dosages produces a slight increase in the height of uterine contractions but reactions are inconstant and the effectiveness may be considered unimportant.

Pituitrin hypodermically in maximal dosages results in a marked increase in the tonicity of the postpartum uterus within three to six minutes. The effects gradually diminish from the early peak and disappear within forty-five to ninety minutes. Second dosages are relatively ineffective if injected earlier than forty-five minutes after the initial dosage. The postpartum uterine response to pituitrin is

directly proportional to the dosage administered. Small dosages produce a moderate rise in tonus and significant increases of the frequency and amplitude of contractions. Maximal dosages produce a spastic uterus with increase in frequency and height of contractions as the tonus diminishes due to passing off of the maximal reactions.

Morphine is capable of significantly reducing the motility and tone of the postpartum uterus, and our observations suggest caution in postpartum medication for pain due to the possibility of uterine relaxation and increased postpartum hemorrhage.

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10515 CARNEGIE AVENUE

Marenzi, A. D., and Gerschman, R.: Phosphorus of the Plasma and Blood During Ether Anesthesia, Rev. Soc. argent. de biol. 10: 64, 1934.

The authors studied the different fractions of phosphorus of the blood before, during and after ether anesthesia. They conclude that the increase of inorganic phosphorus does not come from the hydrolysis of the several compounds of phosphorus in the blood, but is due to the liberation of phosphorus by muscle tissue during anesthesia.

MARIO A. CASTALLO.

Reich, A.: Leucorrhoea, Am. J. Surg. 25: 398, 1934.

The following treatment has been found to be effective in gonorrheal cervicitis and infection by trichomonas vaginalis as well as in the nonspecific infection. The vaginal speculum is introduced and the vagina is dried out. A tablespoon of granulated sugar is put on a small piece of paper, with a tablespoon of ointment of salicylic acid, grains 10; mercuric ointment drachm 2, and zinc ointment up to 1 ounce. Rolled up together in the paper, they are introduced into the vagina followed by a tampon, which is removed in twenty-four hours. No douche is necessary. The sugar and ointment produce a syrupy mixture which is highly bactericidal and remains effective for about one week. At the end of this time a new treatment is given.

J. THORNWELL WITHERSPOON.

HARMFUL EFFECTS OF CERTAIN CHEMICAL SUBSTANCES UPON THE UTERUS OF THE RAT

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THE introduction of chemical substances into the uterine cavity for the purpose of interrupting pregnancy is a practice by no means recent, tincture of iodine having been used for this purpose for half a century. Since about 1930, however, the introduction of various types of irritant pastes (Interruptin and Provocal) has awakened renewed interest in this method of inducing abortion, and apparently the use of these preparations is becoming more and more widespread.

Very little experimental work has been published concerning the action of abortifacients in animals, probably because their widespread use in the human being is comparatively recent and reasonably satisfactory, and also because it seemed unlikely that any knowledge having clinical value could be acquired by such a study. This in view of the great differences in the anatomy and physiology of the human uterus as compared with the uteri of laboratory animals and also in view of the difference in the types of placentation. We fully subscribe to the dictum that in this field, above all others, it is extremely hazardous to apply conclusions reached from the study of one species of animal to the human being, and are not at all certain that anything of clinical importance has been learned in this study. On the other hand, it would seem that where a given agent produces deleterious effects in an animal as hardy as the rat, with its high degree of resistance to infection and relative indifference to trauma, he need not be considered an alarmist who advises caution in the use of similar agents in the human being.

This study, which can only be considered preliminary in scope, had for its object to determine:

1. Which of the substances present in the commonly used pastes was the effective abortifacient.
2. Whether abortion might be induced by other agents.
3. What the after-effects of the abortifacient upon the uterus might be.

Experimental.—In some respects, the rat is an ideal animal for a study of this sort. The uterus is bicornate, with a septum dividing the cervical canal, and it is therefore possible to introduce the agent being studied into one horn, leaving the other horn uninjected as control. Our method was as follows: Rats were smeared, and, when in estrus, placed with

males and breeding observed. When the desired stage of pregnancy had been reached (seven days was used in most instances as at this time the fetuses are visible, although still very small), they were placed under ether anesthesia, a short midline incision from the clitoris headward was made and the uterus examined. A small glass cannula was passed through the cervical canal into one horn, and the material being studied, warmed to body temperature, introduced from a hypodermic

TABLE I. EFFECTIVENESS OF VARIOUS CHEMICAL SUBSTANCES APPLIED TO 252 RATS

Positive: All fetuses in injected horn killed.

Negative: At least one living fetus in injected horn on seventeenth day.

MATERIAL INJECTED (DILUTION)	NUMBER OF ANIMALS	DAY OF INJE- CTION	RESULTS OF INJECTION		APPEARANCE OF UTERUS ON SEVENTEENTH DAY OF GESTATION
			POS.	NEG.	
1. Physiologic saline:					
a.	9	4	6	3	Normal in all cases
b.	26	7	2	24	Normal in all cases
2. Isotonic potassium iodide	9	7	0	9	Normal in all cases
3. Leunbach paste:					
a. Straight	12	7	12	0	Injected horn thin and brown; several with cheesy masses
b. Dil. 2:5	19	7	15	4*	Fair condition, but with walls thin and pale
c. Dil. 1:5	13	7	10	3	As in preceding group
4. Iodine solution:					
a. 1.0 per cent Con.	13	7	12	1*	Practically normal
b. 2.5 per cent Con.	8	7	8	0	Practically normal
5. Potassium oleate					
a. Straight	6	7	6	0	Poor condition, walls thin and pale
b. Straight	8	14	6	2	Examined on twentieth day. Resorption slow
c. Dil. 1:5	4	7	4	0	Fair condition
d. Dil. 1:10	14	7	14	0	Fair condition
e. Dil. 1:10	7	14	7	0	Examined on twentieth day. Resorption more rapid than in "b"
f. Dil. 1:20	7	7	3	4	Good condition
6. Buffer solution					
a. pH 11.29	6	7	2	4	Normal
b. pH 12.06	13	7	8	5	Normal
c. pH 14.0	11	7	11	0	Uteri thin and yellow, masses of cheesy material
7. Corn oil					
a.	13	7	10	3	Resorption slow, condition of uteri fair
b.	9	14	0	9	Apparently no effect when injected so late
8. Hexylresorcinol					
a. Dil. 1:10,000	6	7	2	4	Normal
b. Dil. 1:1,000	7	7	6	1	Normal
9. Hypertonic NaCl					
a. Con. 5 per cent	9	7	2	7	Normal
b. Con. 10 per cent	10	7	4	6	Normal
10. Unmedicated tragacanth jelly	13	7	8	5	Normal

*One living fetus, usually at ovarian end of horn.

syringe attached to the cannula. The amount introduced varied with the size of the uterus, usually 0.1 to 0.2 c.c. comfortably filled the horn, undue distention being avoided. The incision was closed and the animal returned to her cage. On the seventeenth day the animal was again opened under ether and the effect noted. The animal was then permitted to produce and nurse her litter, after which she was given a rest period of from two to three months. She was then bred again, and toward the end of this second gestation period was sacrificed. The appearance and fertility of the horn which had been injected from three to four months previously was noted. Physiologic saline and isotonic potassium iodide solutions were used as controls to make sure that neither the operation itself nor the mere introduction of material into the uterus would cause abortion. The findings from a total of 252 rats are reported in this paper.

Results.—The results obtained are shown in Tables I and II.

TABLE II. RESULTS OF REBREEDING RATS THREE TO FOUR MONTHS AFTER INJECTION OF ABORTIFACIENT CHEMICALS

MATERIAL INJECTED	NUMBER OF RATS REBRED	RESULTS
1. Physiologic saline	22	21 pregnant in injected horn; appearance of all cases normal
2. Isotonic potassium iodide	9	6 pregnant in injected horn; all normal in appearance
3. Leunbach paste		
a. Straight	8	None pregnant in injected horn; all in very bad shape
b. Dilute	14	One pregnant in injected horn; two others looked all right. Other eleven in poor shape, uteri very thin, threadlike; others with large green masses
4. Iodine solution		
a. Con. 1 per cent	11	Seven appeared normal, three being pregnant. Other four very bad, masses of necrotic material representing fetuses of second crop undergoing resorption
b. Con. 2½ per cent	7	None pregnant; much like last four in preceding group
5. Potassium oleate		
d. Dil. 1:10	11	Three pregnant in injected horn; other eight like Leunbach-injected animals
6. Buffer solutions		
b. pH 12.06	9	Seven pregnant in injected horn; others look normal
c. pH 14.0	8	None pregnant. In very bad shape. Resemble Leunbach animals
7. Corn oil	7	Five pregnant; others normal
8. Hexylresorcinol		
b. Dil. 1:1,000	5	None pregnant but look normal
9. Hypertonic NaCl		
a. Con. 5 per cent	7	Five pregnant; others normal
b. Con. 10 per cent	7	Five pregnant; others normal
10. Unmedicated traganth jelly	9	Seven pregnant; others normal

Comment.—As far as the control material is concerned, the introduction of physiologic saline killed the fetuses in six out of nine animals if injection was made on the fourth day. The fetuses were probably not firmly implanted at this time and were washed out. This suggests the early injection of inert material as a possible preventive for pregnancy and this point demands further investigation. In two cases, out of the other 35 controls injected on the seventh day (26 with physiologic saline and 9 with isotonic potassium iodide), the fetuses were killed. We believe this was due to some extraneous factor and is not significant.

The material to which we gave the greatest consideration was Leunbach paste (sold abroad as "Provocal"), since this is the paste most widely used in this country. The *Journal of the American Medical Association* 98: 2155, 1932) contains a report of the Bureau of Investigation concerning this substance. Apparently results abroad are not entirely favorable; the Bureau finding reports of some 25 fatal accidents resulting from its use. In the hands of some obstetricians no untoward results have been noted, while in some clinics, on the other hand, the use of any preparation of this type is prohibited. The formula is given in the article mentioned; it contains soap, iodine, potassium iodide, tincture of benzoin, tincture of myrrh and thymol. "Interruptin," introduced by the German pharmacist Heiser, is apparently a secret preparation, but from the article by H. Wolf (*Monatschr. f. Geburtsh. u. Gynäk.* 88: 442, 1931), is similar in its essential components to Leunbach paste.

We used Leunbach paste in three concentrations, straight, diluted 2 parts of paste to 5 parts water and one part paste to 5 parts water. In its original strength it gave positive results in all of 12 animals; diluted, it was not invariably effective, although the few fetuses left alive were usually well up in the ovarian end of the horn and might not have been reached by the paste. The uteri, upon examination on the seventeenth day of gestation did not look healthy, in many there were masses of greenish, cheesy material while in others the horn looked pale, somewhat yellowish and thin. This effect was much more marked at the end of the four-month rest period when the animals were examined after having been bred the second time. Not one of eight given straight Leunbach paste became pregnant on second breeding and only one of 14 given diluted paste became pregnant. In many of these animals the horn which had been injected several months previously was so small it could hardly be found, histologic examination in several cases showed the epithelium completely gone and the lumen grown together with connective tissue. It is our opinion that many of these uteri could never again have become pregnant, so complete was their destruction. In other cases, where the uterus had apparently not been so badly damaged, nidation had occurred followed by some degree of fetal development, but the fetuses had then died and were undergoing resorption. It should also

be mentioned that 6 of the 44 animals given Leunbach paste died within one month's time; these were the only rats out of nearly 300 that died as a result of the injections. These animals seemed to be suffering from a generalized infection of the entire abdominal cavity, huge greenish abscesses formed, the animals lost weight rapidly and died. The cause of death in the human cases reported in the literature was presumed to be air or soap embolism. We purposely injected air along with soap into several animals and also injected one series with corn oil; no death resulted.

We next attempted to learn which of the constituents of the paste was the active ingredient. Since the base used is soap it seemed advisable to begin with this agent. Neutral potassium oleate was prepared and injected in varying dilutions. When injected on the seventh day, dilutions as great as one part soap in ten of solution gave invariably positive results in a total of 24 animals; in a dilution of 1 to 20, however, the results were not certain. The appearance of these uteri on second breeding after several months rest did not differ greatly from those receiving Leunbach paste, but a higher percentage, three out of eleven, became pregnant the second time.

The next constituent investigated was the iodine. This was used in a 1 per cent solution and in a 2½ per cent solution, dissolved in isotonic potassium iodide. The former was positive in twelve out of thirteen animals and the latter in all of eight. These uteri looked nearly normal when examined the first time, but again, the second breeding attempt showed that serious injury had been suffered, particularly by the group receiving the stronger solution. None of seven animals remained pregnant in the injected horn, several of these horns were enormously distended with a black fluid, while others were filled with cheesy material representing the resorbing fetuses of the second pregnancy. In none of these animals, however, was there the actual destruction of tissue and atrophy of the horn as a whole which resulted from Leunbach paste injection. It is quite possible, we believe, that the horn might have recovered, in time.

It would seem, therefore, that either the soap or the iodine, present in Leunbach paste, would cause abortion. The other ingredients were not investigated.

In studying the possibility of other agents which might have an abortifacient action without the effect of sterilizing the uterus, the first substance that suggested itself was a buffer solution having a fairly high pH, on the assumption that the action of the soap was due to its alkalinity. Solutions having a pH of 11.29, 12.06, and 14 (a tenth-normal solution of sodium hydroxide) were used. Of these, only the latter was reliably abortifacient, but again, its use resulted in horns that were decidedly abnormal after three months' time. Of eight animals rebred,

none carried the fetuses in the injected horn through, although in several cases implantation and some growth of the fetuses had occurred, prior to death and resorption. It appeared as though the resorption of these dead fetuses was hindered by the low degree of vascularity prevailing in the horn; they appeared mummified, but covered with an outer layer of greenish necrotic material. These uteri, on the whole, resembled those of the Leunbach paste-injected animals.

Several shots in the dark were taken in the hope of accidentally stumbling upon some effective agent. Thus, corn oil was used in the hope that it might have a loosening effect upon the placenta; hypertonic saline, in 5 per cent and 10 per cent concentrations, in the hope that it might kill by dehydration; hexyresorcinol and unmedicated gum tragacanth. As will be noted from the tables, none of these agents was reliable. It should be noted that, where positive results were obtained, rebreeding and later examination showed a uterine horn normal in appearance, even though not invariably pregnant.

Discussion.—The most significant finding in this investigation appears to be the long-continued action of the effective abortifacients upon the uterus and the sterility and pathologic state resulting therefrom. As has been stated, it is a question how much of what has been found to occur in the rat would occur in the human being. The rat, for instance, does not abort readily, the fetuses die and are resorbed; in the human being, abortion would tend to eject the agent causing the abortion. Menstruation in the human being would tend periodically to flush out the offending substance. Other essential differences suggest themselves. If, however, there should be any similarity of action and result, it is obvious that an abortion accomplished by the use of such agents as Leunbach paste would be an extremely dangerous proceeding. Even though it only rendered the uterus sterile for a few years, that might mean an extremely unhappy state of affairs for the woman for whom an abortion today may be advisable but with a change in the state of health or finances, a pregnancy next year might be greatly desired. It would at least seem to be the part of wisdom to proceed with caution until a sufficient study of the question of ensuing pregnancies following an abortion by means of these agents has been made. In the meantime further laboratory study of abortifacients upon laboratory animals might well be undertaken, particularly upon primates, or at least upon animals which abort more readily than does the rat.

Thorough histologic study of the uteri and fetuses during the period following the introduction of the abortifacient might also be valuable in indicating its mode of action, whether by killing the fetus directly or by affecting either the uterus or placenta. Such a study might give an indication as to what type of chemical substance could be expected to have an abortifacient action without the deleterious effects described and make a thorough study of such substances less laborious and more

likely to be successful. Also, as has been pointed out, the time factor should be thoroughly studied, as possibly a milder agent might be effective in the pre-implantation stage. The discovery of such an agent or technic might have value as a follow-up measure in the prevention of conception in cases where, for any reason, the efficacy of the contraceptive used was doubtful.

SUMMARY

1. The effective agent in Leunbach paste may be either the soap or the iodine, either substance alone being an effective abortifacient.

2. In the rat, every agent that is dependably abortifacient will, in most cases, render the injected horn sterile for at least a three months' period and will also cause varying degrees of pathologic abnormality.

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HEMORRHAGIC ENCEPHALITIS (NEOARSPHENAMINE) IN OBSTETRIC PATIENTS

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THREE obstetric patients, who died early in the course of anti-syphilitic therapy, have been observed during the past five years. In each instance, the clinical picture was that of hemorrhagic encephalitis, and in two this diagnosis was supported by the anatomic findings at autopsy. Two patients were pregnant near term and one had recently been delivered, so that the appearance of generalized convulsions, followed by coma in the last two, aroused a suspicion of eclampsia. These similarities to the convulsive toxemia of late pregnancy provided interesting problems of differential diagnosis and prompted the following detailed reports of the clinical developments and, in two instances, of the anatomical findings.

CASE 1.—K. R. (Hospital No. D 4452), aged nineteen years, was admitted July 8, 1929, in the eighth lunar month of her first pregnancy. A strongly positive blood Wassermann reaction had been detected by the home physician shortly before admission. On July 12, the Wassermann and Kahn reactions were again reported strongly positive. The date of the initial infection could not be determined.

The family and past histories were not significant.

General physical examination was negative, the pregnancy was progressing normally and corresponded to the menstrual history. There was no edema, the urine was free from albumin, and the blood pressure was 100/55 mm.

Antisyphilitic treatment was instituted two days after admission, and consisted of: July 10, 2 min. of gray-oil, intramuscularly; July 11, 0.2 gm. neoarsphenamine,

intravenously; July 15, 0.4 gm. neoarsphenamine, intravenously; July 17, 2 min. of gray oil, intramuscularly; July 18, 0.4 gm. neoarsphenamine, intravenously; July 22, 0.4 gm. neoarsphenamine, intravenously; July 24, 2 min. of gray oil, intramuscularly; July 25, 0.4 gm. neoarsphenamine, intravenously; July 29, 0.4 gm. neoarsphenamine, intravenously; July 31, 2 min. of gray oil, intramuscularly.

There had been no reaction to the medication except that on July 30 and 31 there was slight headache which did not demand treatment. Weekly examinations had shown the urine to be free from albumin and casts, and the systolic blood pressure had never been higher than 120 mm.

Early in the morning of August 1 (three days after the sixth, and twenty days after the first neoarsphenamine injection), the patient vomited and passed rapidly into a state of spastic paralysis which prevented speech. Responding to direct questions, she indicated that she had a severe headache and that she could not move the arms, which were drawn tightly to the body and were flexed at the elbows with marked pronation of the thumbs. The legs were extended and rigid though the right leg was more spastic than the left. The muscle reflexes were abolished except for the radials which were normal. Chvostek's sign was negative. Sensation was markedly impaired, pain being appreciated only over the chest. The blood pressure was 120/70, and the heart sounds were clear. The temperature was 98.7° and the pulse 86 per minute. The pupils responded poorly to light, but the ocular fundi were normal. The total leucocyte count was 14,300. A catheterized specimen of urine showed no abnormality. Two grains of phenobarbital were given by mouth.

Later on the same day, the spinal fluid, which was under normal pressure, showed 3 cells per c.mm., with no demonstrable globulin or blood: the total protein was 76 and the sugar 135 mg. per 100 c.c. Blood chemistry revealed: Urea nitrogen 10.8, creatinine 1.0, and uric acid 5.0 mg. per 100 c.c. Both the direct and indirect van den Bergh reactions were negative.

Gastric lavage gave little result. One-fourth grain of morphine and 30 gr. of chloral were administered, and tap water was given by rectum.

The patient's condition became rapidly worse during the day. The spasticity gave way to flaccidity, the temperature rose to 104° F., and coma developed. The radial periosteal reflexes remained undisturbed but the knee jerks, biceps and abdominal reflexes could not be elicited, and plantar stimulation provoked flexion. No convulsions were observed. Respiration became irregular and labored, and the temperature rose to 106° (rectal). Death occurred at 3:30 A.M., August 2, respirations stopping a few minutes before the heart. Delivery had not been effected.

Complete postmortem examination was begun six hours after death. The pathologic diagnoses were: moderate congestion of the lungs; marked degeneration of the renal tubules; acute encephalitis, toxic, arsenical.

Throughout the brain there was marked involvement of the capillaries, which were practically plugged with fibrinous thrombi, containing many leucocytes. The fibrin, which was adherent to the vessel walls, formed in some places a loose reticulum and in others a solid hyalinized plug. In certain areas, the endothelium of the vessel walls was edematous and showed proliferation and desquamation into the lumina. Polymorphonuclear leucocytes were seen invading the vessel walls and infiltrating the surrounding tissues. The Virchow-Robin space contained a delicate fibrinous exudate.

Small recent punctate hemorrhages were present in several areas. The blood was largely in the perivascular spaces and in the surrounding brain tissue. Edema was marked, especially in the white matter of the internal capsule and the corpus callosum. The perivascular spaces were widely dilated, the supporting tissues of the white matter were thinned out, and numerous small cystic areas were present, some of which had coalesced. The cerebral lesions evidently represented an acute, toxic

encephalitis, probably due to arsenical poisoning. The damage was apparently very recent so that there had been insufficient time for striking morphologic changes.

CASE 2.—I. B. (Hospital No. F 8877), aged twenty-two years, was admitted Oct. 19, 1931, in the eighth month of her first pregnancy. On admission, the urine was normal, the blood pressure 120/80, and general physical examination revealed no gross abnormalities. On October 26, smears from the urethra and cervix showed gonococci, and local treatment was instituted. On October 19, and again on October 21, the blood Wassermann reaction was reported strongly positive to both alcoholized and cholesterinized antigens, and the Kahn test was likewise strongly positive. There were no clinical signs of syphilis, but the spinal fluid Wassermann was positive. The hemoglobin was 90 per cent, and the total leucocyte count was 9,300. The patient was treated as follows: October 27, 0.2 gm. neoarsphenamine, intravenously; October 30, 0.4 gm. neoarsphenamine, intravenously; November 2, 0.4 gm. neoarsphenamine, intravenously.

Following the first two injections there was considerable pain and tenderness in the arms around the injection sites, probably due to extravasation of the solution into the subcutaneous tissues, but no evidence of any general reaction.

On November 3, the day after the third injection (six days after institution of treatment), the patient was severely nauseated and complained of abdominal pain. Headache, backache, and dizziness appeared on the next day, November 4. Intermittent abdominal pains continued, and early in the morning of November 5, the cervix was found by rectal examination to be 2 to 3 cm. dilated. In view of the small size of the fetus, $\frac{1}{4}$ gr. of morphine was given. When the hypodermic injection was made, the patient screamed and immediately developed a generalized convulsion, during which she scratched her face and bit her lips. Urine obtained by catheter contained no albumin or abnormal cellular elements. There was no edema. After the convulsion, the patient was disoriented and stuporous. The deep reflexes which had been slightly hyperactive became markedly diminished. There was no rigidity of the neck and no skin eruption. The temperature rose from normal to 102° F. A second generalized convulsion occurred at 4:00 A.M.

During the late morning of November 5, almost continuous twitching appeared together with a rapid succession of convulsions, five in all, which varied markedly in extent. The first of this series was generalized, the second almost entirely confined to the right side, while the third involved only the left side. The blood pressure shortly after a convulsion was 105/50. The ocular fundi were essentially normal. After this series of convulsions the patient became comatose and had one more generalized convulsion before she died, undelivered, at 9:30 P.M. Treatment consisted of intravenous injections of sodium thiosulphate and of glucose solution. Autopsy was not permitted.

It was felt that the patient probably died from hemorrhagic encephalitis resulting from the intravenous arsenical treatments which she received because the clinical picture was so similar, except for the convulsions, to that observed in the first case, where the diagnosis had been confirmed by postmortem findings. The absence of edema and of hypertension together with the nature of the convulsions was entirely unlike eclampsia. We have never seen an eclamptic convulsion which was other than generalized, and doubt whether unilateral seizures ever appear in this disease.

CASE 3.—A. J. T. (Hospital No. H 12,970), aged twenty-two years, a secundigravida, was admitted on Nov. 27, 1933, in the tenth lunar month of a normal pregnancy. The previous pregnancy had terminated in December, 1932, as a spontaneous miscarriage at fourteen weeks. Blood Wassermann reactions on November 28 and on November 30 were strongly positive (++++), as was the Kahn test. The spinal

fluid Wassermann reaction was positive (+++++) on November 28. Urine passed on the same day was normal, and the blood pressure was 112/88. Antisyphilitic treatment was given as follows: December 1, 0.2 gm. neoarsphenamine, intravenously; December 4, 0.4 gm. neoarsphenamine, intravenously, 2 min. of gray oil intramuscularly; December 7, 0.4 gm. neoarsphenamine, intravenously.

The patient was delivered spontaneously on December 8, at 12:43 A.M., after a labor lasting one hour and thirty-eight minutes. The child, which weighed 3,193 gm. at birth, appeared grossly normal. The Wassermann reaction on the cord blood was strongly positive (+++++), but the Kahn test was negative. Roentgen ray films of the long bones revealed no evidence of congenital syphilis. The child was discharged on December 21, 127 gm. above birth weight.

Within a few hours of delivery, the patient's temperature rose to 100.6° F., but returned to normal within twelve hours (delivery reaction?). On December 9, there were no complaints except for a few after-pains. The following day the patient complained of a feeling of general malaise and responded slowly to questions. The pulse was 128, the temperature 100° F., and the blood pressure 145/105. The urine showed a moderate trace of albumin with numerous finely granular casts and many pus cells, and occasional red blood cells. One hundred and fifty cubic centimeters of 50 per cent glucose solution were given intravenously.

Throughout the afternoon she remained sluggish and became progressively less reactive. At 4:00 P.M., unconsciousness supervened, and at 4:50 P.M. there was a generalized convulsion followed by marked cyanosis with definite respiratory difficulty. Three more generalized convulsions followed in rapid succession before the patient was brought under the influence of $\frac{1}{4}$ gr. of morphine sulphate, and $7\frac{1}{2}$ gr. of sodium amytal. Lumbar puncture showed the spinal fluid under normal pressure, but the Pandy reaction was two-plus, and there were 20 lymphocytes per cubic millimeter. The blood pressure had risen to 160/110 mm. Blood chemistry revealed: uric acid, 5.6; urea nitrogen, 11.9; and creatinine, 1.6 mg. per 100 c.c., while the CO₂ combining power was 49.1 vol. per cent, and the van den Bergh was 0.1. The biceps, triceps, knee-jerks, and tendon achilles reflexes were hyperactive, but the abdominal reflex was absent. Plantar stimulation provoked flexion with slight extension of the great toes. Bilateral ankle clonus was present. Because of the respiratory difficulty, oxygen was administered by nasal tube.

At 8:55 P.M. $\frac{1}{60}$ gr. of atropine sulphate was given to combat excessive mucous secretion in the upper respiratory tract. It was noted that the neck was moderately stiff. Urine obtained by catheter at 9:15 P.M. showed a moderate trace of albumin, many finely and coarsely granular casts, and occasional red and white blood cells. The blood pressure was 120/75 mm., respirations were 24 and the pulse 100 per minute. Twenty grains of chloral hydrate and 40 gr. of sodium bromide were given by rectum.

On December 10, at 12:30 A.M., the temperature was 105° F. (axillary), the pulse 140 to 160 per minute, and the blood pressure 120/40. Death occurred at 1:35 A.M., the heart stopping one minute after respirations had ceased. The axillary temperature shortly before death was 107° F.

Clinical diagnoses included: (1) A vascular type of neurosyphilis, (2) hemorrhagic encephalitis, and (3) postpartum eclampsia. The picture so closely resembled that of the previous proved case of hemorrhagic (arsenical) encephalitis (Case 1) in (1) the time of onset in relation to the last injection of neoarsphenamine, (2) the clinical determination of marked central nervous system disturbances, and (3) the rapidly fatal outcome, that this seemed the most probable diagnosis. There had been, however, none of the usual prodromes, such as nausea and vomiting, headache, or dizziness. Eclampsia was suggested by the presence of a slight hypertension and the determination of a moderate albuminuria and cylindruria, even in

the absence of edema, but the late appearance of the first convulsion (thirty-nine hours after delivery) and the absence of earlier evidence of a toxemia of late pregnancy argued against this diagnosis.

Necropsy was performed seven hours postmortem. The final pathologic diagnoses included: bronchopneumonia, postpartum uterus, syphilitic aortitis, chronic syphilitic leptomeningitis, and hemorrhagic (arsenical) encephalitis.

The brain appeared normal grossly and the convolutions were well defined. The cerebral vessels were injected, but the walls were thin and the lumina were not occluded. The meninges were normal and showed no localized thickening.

Microscopically, there was considerable congestion of the meningeal vessels but no hemorrhages in the cerebrum. In certain areas, especially over the cord, the meninges were thickened and infiltrated with chronic inflammatory cells, chiefly lymphocytes and plasma cells. Edema of the brain tissue was questionable. Some of the cerebral vessels, more especially those in the basal ganglia, showed perivascular infiltration with leucocytes. A few very small hemorrhages were present, for the most part in the basal ganglia, where certain small vessels contained polymorphonuclear leucocytes, some of which appeared to be within the vessel wall rather than perivascular. This was interpreted as evidence of an arteritis.

The typical history for an arsenical reaction and the finding of minute hemorrhages in association with a definite arteritis, although the presence of edema was doubtful, seemed to justify the diagnosis of arsenical encephalitis. The inability to detect arsenic chemically in the blood or brain tissue may be explained by a fixation of the metal in tissues other than the brain after its removal from the blood stream.

SUMMARY

Three young women, aged respectively nineteen, twenty-two, and twenty-two years, died during late pregnancy or shortly after delivery, in the course of antisyphilitic therapy directed at latent syphilis detected by routine blood Wassermann tests. In two instances, hemorrhagic encephalitis was demonstrated postmortem, while in the third the clinical picture made the diagnosis reasonably certain. Neoarsphenamine was employed in each case; six injections totaling 2.2 gm. in Case 1, and three injections totaling 1.0 gm. in each of the other two. In addition, four injections of gray oil (two minims each) were given to the first patient and one similar dose to the third patient.

In each instance the initial dose was within the limit usually recommended and succeeding doses were not large, being smaller than the maximum dose (0.45 gram) recommended by the Council of the German Public Health Service,¹ but somewhat larger than the maximum recommended by Klasten² for use in pregnant women. Moreover, injections were made twice weekly, instead of once each week as is commonly advised. It should also be noted that in two instances the spinal fluid Wassermann reaction was positive despite absence of clinical evidence of cerebrospinal syphilis. There is no good reason to believe that such patients are especially liable to the appearance of encephalitis.

In each instance, cerebral symptoms of arsenical poisoning developed within seventy-two hours after the final injection of neoarsphenamine, and death occurred within three days of the initial manifestations, or

on the third to the fifth day after the last injection. Two patients developed convulsive seizures, which naturally suggested puerperal eclampsia, a condition which must obviously be considered whenever convulsions appear in the latter semester of pregnancy or shortly after delivery. In Case 2, the bizarre character of the convulsions, and, in Case 3, the anatomical findings clearly removed this possibility.

DISCUSSION

These three fatalities in a relatively small series of syphilitic pregnant women under treatment with presumably the safest of the modern arsenicals naturally raises the question of increased susceptibility to the toxic effects of arsenic during gestation. Nowhere can we find this subject discussed with any thoroughness, and it has seemed advisable to review briefly the available literature.

Cole and his collaborators³ are of the opinion that young adults generally are more susceptible to the toxic effects of arsenical injections, and that women are more susceptible than men, an opinion which is also shared by Klaften,² Pritzi,⁴ and Ireland.⁵ The danger seems likewise to be greater early in the course of treatment (Ireland,⁵ Cole et al.,³ and Phelps and Washburn⁶) with symptoms more commonly appearing after one to four injections. Cole's³ statistics indicate that those with latent syphilis are more likely to develop reactions than are those with early lesions, and the common finding in pregnant women is a latent infection, which is discovered only by routine serologic tests.

Klaften,² Pritzi,⁴ McKelvey and Turner,⁷ and Clason⁸ apparently believe that pregnancy increases the danger of serious reactions, while the first-named² attributes a pernicious influence to menstruation and recommends a reduced dosage during these two physiologic states. Gammeltoft⁹ quotes Kristjansen as saying that among all patients treated with salvarsan at Rudolph Bergh's Venereological Hospital during a ten-year period four or five died from salvarsan poisoning, and three were pregnant women. Klaften² quotes Meirowsky as having collected data on twenty-three salvarsan fatalities among women, fourteen of whom were pregnant. This author likewise states that he has observed women who showed salvarsan reactions while pregnant, but who after delivery were given the same drug without observable bad effects. In the past five years there have been eight deaths at the University Hospitals from hemorrhagic (arsenical) encephalitis; all of the patients were females and of these three were pregnant. On the other hand, McCord¹⁰ says: "With an experience of many thousands of doses of all kinds of arsenical preparations given to pregnant women, I have never seen a reaction that approached a fatality: I rarely see a reaction of any kind." The fortunate experience of this observer may be attributed to the fact that his patients are all colored women, who, according to certain investigators, Cole et al.,³ are more immune to the common toxic effects than are white women.

Pritzi⁴ believes that the danger of toxic reactions increases as term is approached, and that the increased susceptibility is due to changes in the body colloids and lipoids, which are well known to develop during gestation. Eastman¹¹ has, however, pointed out that the placenta acts as a storage center for injected arsenic, which is then gradually set free in the blood for long periods after the injection, and it is possible that this factor is significant, since it involves a more or less continuous introduction of arsenic into the system. This phenomenon is utilized to explain the relatively greater therapeutic efficiency of small doses of the arsenicals given to

pregnant women, and may also bear some relation to their apparently greater susceptibility to its pernicious effects. It must also be remembered that pregnancy presumably produces a certain amount of capillary alteration and that the lesions of arsenical encephalitis are, according to Ireland⁵ "doubtless produced by capillary vascular injury or thrombosis." Scott and Moore¹² have suggested that the destructive and dilating action of arsphenamine on the blood vessels is not counteracted by epinephrine, which is deficient because of the arsenical destruction of the suprarenals, an opinion which is concurred in by Brittingham and Phinizy.¹³ They also believe that "the delayed arsphenamine reaction is nothing more than an arsenic poisoning due to the liberation of poisonous trivalent arsenic from the faultily eliminated arsphenamine."

There is considerable difference of opinion concerning the possible bad effects of the modern arsenicals upon pregnancy. Gammeltoft¹⁴ believes that the salvarsan series of drugs does not cause abortion, but quotes Gougerot, Merklen, Wolf, and Neel as expressing an opposite opinion. Klaften² doubts a cause-and-effect relationship, although he has seen abortion follow administration of the arsenicals, while McKelvey and Turner⁷ insist that arsphenamine does not increase the incidence of abortion and is without deleterious effects upon the fetus.

The Council of the German Public Health Service,¹ in setting up criteria for the use of arsphenamine preparations recommends especial care in certain organic diseases and in pregnancy and advises initial trial doses, with full doses only if the drug is well borne. Klaften² and Pritzi⁴ recommend that the maximum dose of neoarsphenamine for pregnant women be 0.3 gm., with proportionate maxima for the other arsenicals. Stokes et al.,¹⁵ in outlining a "standard treatment procedure in early syphilis," likewise recognize the need for care in the treatment of pregnant women if reactions are to be avoided.

It is well recognized that, even under ideal conditions and with every precaution satisfied, reactions will follow the intravenous use of antisyphilitic arsenicals. Excluding early febrile sequelae, such as "endotoxic reactions" due to the liberation of the "syphilitic toxin" from the spirochetes by the destructive action of the drug, and the "water fever" due to pyrogenic factors in the water used for solution of the drug, Parnell and Fildes¹⁶ found that among 6,588 injections of neoarsphenamine given to 1,250 patients there were 78 reactions, slightly over 1 per cent. The greatest danger was during the first series and after the second, third or fourth doses, and particularly after the third, when almost one-half of the reactions occurred. Cole et al.³ in "very close to 78,350 injections" of the various arsenicals found that 15.3 per cent of the 1,212 patients studied showed one or more arsenical complications of treatment (19 per cent of the latent and 14.3 per cent of the early cases). There were twelve fatal cases: "six from hemorrhagic encephalitis, five from crustaceous dermatitis exfoliativa, and one from acute severe arsenical hepatitis, all cases treated less than six months." Eight of the twelve fatal cases had received no more than four injections. Ireland⁵ noted reactions in 15 per cent of the female and 8 per cent of the male patients in his series of 2,100 cases, but seemingly had no fatalities. Klaften² quotes figures to show that fatal reactions occur in from 1 in 20,000 to 1 in 30,000 injections of neoarsphenamine, provided the maximum dosage is not more than 0.6 gm. Phelps and Washburn⁶ reviewing 272,354 injections recorded one death in 16,021 injections in their entire series, with the ratio 1 in 22,625 for arsphenamine and 1 in 14,844 for neoarsphenamine.

The more dangerous of the late reactions are exfoliative dermatitis, stomatitis, acute yellow atrophy of the liver (jaundice), and hemorrhagic encephalitis¹⁷ with the last responsible for at least one-half of all deaths.¹⁸ Phelps and Washburn⁶ record one fatality from hemorrhagic encephalitis for every 1,171 patients treated,

or one for every 23,000 injections. These investigators record twenty deaths from this complication, with ten occurring after the second injection, as against four deaths from dermatitis and none from acute yellow atrophy of the liver.

The symptomatology of arsenical hemorrhagic encephalitis varies considerably, but there is usually early evidence of involvement of the central nervous system, with tonic and clonic convulsions and coma predominating. The convulsive seizures may be generalized or unilateral and are commonly followed by coma which terminates in death. More rarely there may be delirium with fever, vomiting, and shock. Prodromes, in the form of nausea and vomiting, headache, restlessness, and fever are frequently observed, but their serious significance is not appreciated until other symptoms supervene. In a recent case of exfoliative dermatitis developing shortly after delivery, the prodromes aroused a strong suspicion of early encephalitis, but on the following morning the development of a typical skin rash was associated with rapid disappearance of the mild nervous phenomena. Other symptoms and signs, as enumerated by Phelps and Washburn⁶ include: prostration, tachycardia, nervousness, congestion of the throat and eyes, backache, severe abdominal pain, diarrhea, swelling of the posterior cervical glands, delirium, cyanosis, and slight muscular twitchings. In some instances, there may also be a paralysis of certain muscle groups, of a flaccid, or spastic character.

In pregnant and recently delivered women, the appearance of convulsions and coma naturally arouses a suspicion of eclampsia. However, the usually atypical character of the convulsions, the absence of hypertension and albuminuria, and the history of intravenous arsenical injections within a few days should suggest hemorrhagic encephalitis. Moreover, signs of serious central nervous system involvement quickly appear; the deep reflexes are at first hyperactive but soon become greatly diminished or absent, Babinski's sign may be positive, squint may appear, disturbances of sensation may be detected, disorientation may be observed, and ankle clonus may be elicited. Final diagnosis in doubtful cases may rest upon the postmortem demonstration of edema and small hemorrhages in the brain and spinal cord, as well as in the skin, pericardium, and various viscera. Hemorrhages into the central nervous system alone are pathognomonic; they usually appear as small punctate extravasations of blood around the capillaries, but occasionally the coalescence of several such small hemorrhages produces a larger hemorrhagic area. Hyaline thrombosis of the capillaries is also frequently observed.

Death usually occurs within ninety-six hours, but Dickens,¹⁹ Phelps and Washburn,⁶ and Klaften² have reported patients with symptoms suggesting hemorrhagic encephalitis who recovered completely. Treatment commonly consists in the exhibition of hypnotics to control the convulsions, venesection, spinal puncture, and the intravenous injec-

tion of hypertonic solutions of glucose or sodium thiosulphate, but it is doubtful whether anything has much effect upon the course of the disease.

CONCLUSIONS

Three cases of hemorrhagic encephalitis are recorded in women near term or shortly after delivery, when the disease closely resembles eclampsia, in that it is commonly associated with convulsions and coma.

From our experience and from a review of the literature, it seems that pregnant women are more susceptible to the deleterious, as well as to the beneficial, effects of antisyphilitic treatment by the modern arsenicals than are other individuals. This susceptibility is more marked (1) during the first course of therapy, (2) in latent rather than in early syphilis, and, (3) in the last trimester of pregnancy.

The clinical picture, as we have observed it, was varied and may be confusing, but positive diagnosis can be made by pathologic changes in the central nervous system, more especially by the presence of scattered punctate hemorrhages around the smaller vessels, and usually by an associated edema.

Treatment was of little avail, death occurring within three days after the first toxic manifestations in each of our cases. Intelligent prophylaxis demands that great care be exercised in giving a first course of antisyphilitic arsenical therapy to a woman with latent syphilis in the latter months of pregnancy.

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THE THERAPEUTIC VALUE OF ANTUITRIN-S IN MENOMETRORRHAGIA

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IN RECENT years no aspect of medicine has interested the profession to a greater degree than that relating to the function of the glands of internal secretion. Particularly in gynecology the advance in our knowledge has helped to give us a better understanding of the physiology of the generative organs. The demonstration of an ovarian active principle, the female sex hormone, in the circulating blood by Frank and his coworkers¹ and almost simultaneously by Loewe² represented the beginning of the modern advances. Further impetus was given hormonal studies in this field by the work of Allen and Doisy³ who established the biologic test for the female sex hormone, and by Aschheim-Zondek⁴ who isolated the prepituitary hormone. Since that time the volume of work has become so vast that it is almost an impossibility to follow the extensive literature that has arisen. Although the facts already established have helped our understanding of the physiology of the female genital tract, much remains to be cleared up. It is heartening to observe that the preponderance of published work is the result of laboratory experimentation. From the clinical angle attempts are being made to apply various hormone preparations found active in laboratory animals to human beings. The results published have already implanted in the mind of the medical profession to a considerable degree the usefulness of various endocrine preparations on the market at the present time. That they are extensively used is evident.

In previous papers^{5, 6} we published our observations on the clinical results from the use of amniotin and theelin in the menopause. Some patients were improved but most were not. The only really favorable results were obtained in kraurosis vulvae where female sex hormone preparations definitely gave relief from itching during the period of treatment. In the discussion of a paper by E. Novak at the American Gynecological Society, one of us (S. H. G.) reported 24 cases of menometrorrhagia treated with antuitrin-S with no striking therapeutic effect.

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We wish at this time to report the results obtained with antuitrin-S* in 14 additional cases of menometrorrhagia; the preparation, antuitrin-S titers, in the fresh state, to 100 R.U. per c.c. In all, 14 patients were treated for a period of three months. The substance was given by intramuscular injection 3 times weekly beginning with a dose of 3 c.c. per injection. Greater doses did not seem to us to be justifiable, especially as almost without exception the patients complained of fever and generalized pains after receiving large doses. The cases were selected with the express purpose of determining the efficacy of the preparation used, and for that reason no other therapy was given, with the possible exception of hygienic measures instituted in 2 cases. The series was limited because the cases were selected to rule out any lesion other than that associated with true functional menometrorrhagia.

RESULTS

The results are classified according to the improvement noted. Table I shows the essential data. For the sake of accuracy those patients who showed even the slightest improvement were recorded as "improved." Actually, 2 patients were definitely benefited (M. C. and H. E.). The rest either were not relieved of the bleeding or the relief was negligible. It can be seen that here impersonal interpretation may be exceedingly difficult, and that a rigid sense of values must be brought into play to arrive at acceptable conclusions.

Of the 2 cases showing definite improvement, one (M. C.), was a virgin, eighteen years old, who had bled continuously for thirty-three days before treatment was begun, and who stopped bleeding almost immediately after the injections were instituted. Relief was striking. Of greater interest, however, is the fact that the patient remained amenorrheic for three and one-half months, even after treatment was discontinued. The other patient who showed definite improvement (H. E.) was forty-five years old, was markedly asthenic, and here general hygienic measures had to be included as part of her treatment. Of the remaining patients, 7 were not at all improved, and the other 5 were only slightly relieved. To qualify the term "slight improvement," it may be mentioned that it refers to shortening of the duration of the periods of bleeding to a minor extent. It cannot under any circumstances be interpreted as demonstrating an actual beneficial effect.

DISCUSSION

As has been mentioned, in our series only 2 cases showed definite improvement. The first (M. C.) was amenorrheic for three and one-half months after treatment was begun. We wish to emphasize that cases of this type are very likely unduly to prejudice the physician in

*We are indebted to Parke, Davis & Co., for a liberal supply of the material.

TABLE I

PATIENT	AGE	PARITY	SYMPTOMS	PELVIC FINDINGS	NUMBER OF INJECTIONS AND DOSE	RESULTS	REMARKS
G. K.	25	0	Menometrorrhagia	Uterus slightly enlarged and thick	24 injections up to 6 c.c.	Improved at first. Bleeding recurred	Initial improvement then recurred
A. D.	23	0	Menometrorrhagia	Small, hypoplastic uterus otherwise negative	10 injections up to 6 c.c.	No improvement	Patient subsequently stopped bleeding spontaneously
L. P.	44	x	Metrorrhagia	Essentially negative	24 injections up to 6 c.c. per injection	Very slow improvement	Patient became pregnant while under treatment
M. C.	18	0	Metrorrhagia	Virgo essentially negative later cystic right ovary felt	30 injections up to 6 c.c.	Stopped bleeding. Improved	Became completely amenorrheic for three and a half months
R. D.	44	ii	Metrorrhagia	Irregular scarring of cervix. Uterus slightly enlarged	37 injections up to 6 c.c.	No improvement	
D. E.	45	iii	Menorrhagia	Essentially negative	30 injections up to 6 c.c.	No improvement	
I. B.	34	0	Metrorrhagia		38 injections up to 6 c.c.	No improvement	
P. S.	40	vii	Menorrhagia	Essentially negative	29 injections up to 6 c.c.	Slight improvement	Patient had menopause
H. E.	45	0	Metrorrhagia	Essentially negative	14 injections up to 6 c.c.	Improved	Patient markedly asthenic. Received general hygienic treatment as well
M. M.	34	i	Menometrorrhagia	Right adnexa slightly cystic	30 injections up to 6 c.c.	Improved at first then bleeding recurred	
C. N.	26	v	Metrorrhagia	Ventroflexed uterus, otherwise negative	42 injections up to 6 c.c.	Some improvement	Patient asthenic. Improvement associated with general hygienic measures
J. N.	36	ii	Menorrhagia	Retroversion	20 injections up to 6 c.c.	No improvement	
R. S.	46	0	Metrorrhagia	Essentially negative	34 injections up to 6 c.c.	No improvement	
M. R.	30	ii	Menorrhagia	Slightly enlarged uterus	9 injections up to 4 c.c.	Very slight improvement if any	

favor of any material which he may use. There is a tendency to forget that such a cycle of events may occur without treatment of any kind. The "coincidence" factor must not be regarded too lightly. In the other case that showed marked improvement, hygienic measures which were included in the treatment due to the patient's marked asthenia, may have played more than a casual rôle.

In contrast to the above series, we wish to call attention to a control group of menometrorrhagia cases which have shown improvement under a regime of such simple measures as ergot, short hot douches, or following no active treatment at all. We emphasize this because the factor of coincidence, as had been mentioned, is of great importance.

It is interesting to note that our results are in marked variance with reports to be found in the literature. Prior to 1925, there are repeated references to the efficacy of endocrine preparations long since proved inert. The era when "corpus luteum extract" was in vogue is also not too remote. The use of prepituitary and female sex hormone preparations is the latest development. Careful scrutiny of the literature brings to light facts which are not only interesting but also actually astounding when subjected to analysis. Tables II, III, and IV represent a cross-section of the recent literature and are fairly representative of the claims made for various endocrine products. At the outset one is struck by the great variety of conditions in which the prepituitary and female sex hormones have been applied. Although these preparations properly belong to the gynecologic field, it is astonishing to see that not only are they in use in entirely unrelated conditions, but also good results are actually reported. Thus Bengston⁷ and Kohn⁸ have found the prepituitary hormone efficacious in alopecia, practically always in males.

In the abnormalities of the female genital system the reports are on the whole, favorable. In the amenorrheas and oligomenorrheas, as Table II shows, the hormone preparations have apparently helped to regulate the cycle to a greater or lesser degree. The results, however, are far from conclusive. For example, Sevringhaus and Thornton⁹ report improvement in 10 of 23 patients treated with follutein or antuitrin-S. From such a report some doubt as to the value of the therapy must certainly be entertained. Female sex hormone preparations alone have yielded somewhat better results, which probably accounts for the present popularity of this material in amenorrheic states. However, even if it were possible to produce menstruation by the use of hormone preparations in all cases, it is questionable whether the constant injections necessary are justifiable. In our opinion careful explanation of the individual's condition, with reassurance and perhaps advice as to general hygiene should be all that is necessary. Occasionally a marked asthenia, hypothyroidism, or obesity is found to be the underlying cause of the amenorrhea. One of us (S. H. G.)¹⁰

TABLE II. RESULTS OF USE OF FEMALE SEX HORMONE IN VARIOUS CONDITIONS

AUTHOR	MENOPAUSE	AMENOR- RHEA	KRAUROSIS	HABITUAL ABORTION	MENO- METHOR- RHAGIA	DYSMENOR- RHEA	PSYCHO- NEUROSIS	HEMO- PHEIA	STERILITY
Geist and Spielman ^{5, 6}	Equivocal results	Poor	Temporary relief of itching						
Sevringhaus and Thornton ⁹	Good								
Johnstone, Wiesner, and Marshall ¹⁴		Good		Good	Good				
Ehrhardt ¹⁵		Good 70%			Good				
Hamblen ¹⁶	Good	Good				Good	Good 30%		
Schmidt and Anselmino ¹⁷	Poor	Poor	Good in eczema						
Barach ²⁰	Good	Good							
Hall ²¹	Good	Good							
Birch ²²								Good	
Stetson, Forkner, Chew, Rich ²³								Poor	
Hirst ²⁴									Good in 5 of 12
Szego ²⁵			Good in eczema						

TABLE III. ANTERIOR PITUITARY-LIKE HORMONE IN VARIED CONDITIONS

AUTHOR	MENO- METROR- RHAGIA	ALOPECIA	AMENORRHEA	HIRSUTIES	DYSMENOR- RHEA	HABITUAL ABORTION	BREASTS	PSYCHIC
Geist and Spielman ^{5, 6}	Poor results							
Bengston ⁷		Good results						
Sevringhaus and Thornton ⁸			Good in 50 per cent	Poor results				
Laroche and Simmonet ¹²			Good		Good			
Novak ¹³	Good results		Good in some					
Johnstone, Wiesner, Marshall ¹⁴	Good F. S. H. and A. P. R.		Good result F. S. H. and A. P. L.			Good results F. S. H. and A. P. L.		
Ehrhardt ¹⁵	Good F. S. H. Equivocal A. P. H.		Good				Galactagogue	
Hamblen ¹⁶	Equivocal		Good F. S. H. and A. P. L.					Good 30 per cent
Witherspoon ¹⁸						50 per cent good		
Barach ²⁰	Good results climacteric		Good F. S. H. and A. P. L.					

in a study of normally menstruating women has pointed out the marked variations in the menstrual cycle which may occur in perfectly healthy young women. Fluhmann¹¹ also calls attention to these variations.

In the menometrorrhagias the results are conflicting. Laroche and Simmonet¹² warn against using the prepituitary hormone, while Novak¹³ finds it useful. Johnstone, Wiesner, and Marshall¹⁴ obtain improvement with a combination of anterior pituitary and female sex hormone, while the results of Ehrhardt¹⁵ and of Hamblen¹⁶ are equivocal. Schmidt and Anselmino¹⁷ do not find hormonal therapy efficacious in menstrual disturbances, but obtain good results in climacteric eczema, urticaria, pemphigus, pruritis, and arthritis deformans. These varied opinions are only mute testimony to the fact that hormonal therapeutics at the present time leaves much to be desired. It may be mentioned in passing that we believe that snake venom therapy as reported by Peck and Goldberger¹⁹ in functional bleeding is probably the most efficacious treatment in use at the present time.

TABLE IV. COMPARISON BETWEEN RESULT OF TREATMENT IN SIMILAR CONDITIONS WITH DISSIMILAR SUBSTANCES

AUTHOR	MENO- METROR- RHAGIA	AMENOR- RHEA	HABITUAL ABORTION	DYSMENOR- RHEA	PSYCHIC SYMPTOMS
Geist and Spiel- man ^{5, 6}	Poor A. P. L.	Poor F. S. H.			
Novak ¹²	Good A. P. L.	Good in some A. P. L.			
Hamblen ¹⁶	Equivocal A. P. L.	Good F. S. H. and A. P. L.		Good F. S. H.	30% good F. S. H. and A. P. L.
Johnstone, Wiesner, Marshall ¹⁴	Good F. S. H. and A. P. L.	Good F. S. H. and A. P. L.	Good F. S. H. and A. P. L.		
Ehrhardt ¹⁵	Good F. S. H. Equivocal A. P. L.	Good F. S. H. Good 70% A. P. L.			
Schmidt and Anselmino ¹⁷		Poor F. S. H.			
Barach ²⁰		Good F. S. H.			
Hall ²¹		Good F. S. H.			
Sevringhaus and Thornton ⁹		Good 50% A. P. L.			
Laroche and Simmonet ¹²		Good A. P. L.		Good A. P. L.	
Witherspoon ¹⁸			Good A. P. L.		

Little need be said regarding the other conditions treated and favorably reported upon. Witherspoon¹⁸ used the prepituitary hormone in 12 cases of threatened abortion treated in the hospital, where his criteria of suitability for treatment were "cramps, uterine bleeding, and two finger dilatation of the cervical os, through which the uterine contents can be palpated." Six of the 12 patients aborted while under treatment. He claims 50 per cent cures although of the "cures" 4 patients subsequently aborted after leaving the hospital. In habitual abortion Johnstone, Wiesner, and Marshall¹⁴ obtained good results with both hormones. The patients, however, were kept in bed during the interval of the expected periods. Such reports are misleading.

For any therapeutic measure to be acceptable, exact and unquestioned results must be obtainable in a high percentage of cases. When sex hormone preparations can show the definite and striking effects in the human being that insulin, adrenalin, and pituitrin do, then and then only may they be welcomed as part of the physician's armamentarium.

SUMMARY AND CONCLUSIONS

1. In 14 cases of menometrorrhagia exhibition of the prepituitary-like hormone in the form of antuitrin-S was associated with improvement in two cases only.

2. A survey of the literature shows such varied and conflicting opinions, that the present widespread use of "endocrine" products in menstrual disturbances seem to us to be unwarranted.

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100 EAST 74TH STREET

145 WEST 86TH STREET

THE ORIGIN OF CHORIONEPITHELIOMAS AND OF EMBOLI
FROM TROPHOBLASTIC FRAGMENTS ENCLOSED
IN THE MYOMETRIUM

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SINCE the early writings of Sanger¹ concerning that type of neoplasm which he chose to term "deciduoma malignum," there have been frequent appearances in the medical literature of articles relating to this subject. In 1898 et seq. Marchand's noteworthy contributions^{2, 3} greatly clarified the field by quite conclusively demonstrating the placental origin of this neoplasm. He indicated the striking similarity between the neoplastic cells composing the tumor and the syncytial and Langhans cells of normal chorionic villi, and designated the neoplasm "chorionepithelioma." Recently, reports^{4, 5, 6} of positive Aschheim-Zondek reactions obtained from the urine of patients with chorionepithelioma have proved further the close relationship between this neoplasm and normal placental tissue.

Numerous articles^{7, 8, 9, 10} offering a study of the pathogenesis of chorionepithelioma by means of various case reports have established the clinical manifestations of the disease. Most of these patients have presented neoplastic tissue easily accessible for biopsy. An examination of tissue curetted from the uterus has established the diagnosis of chorionepithelioma. However, certain patients, afflicted with this neoplasm, have not been adaptable to this type of study. Uterine curettements have failed to reveal neoplasm. Consequently, the condition has been misinterpreted, and therefore mismanaged. We propose to review two cases of this type, indicating the inherent possibilities of error in diagnosis and resultant mismanagement, with the hope that subsequent similar situations will be approached more intelligently.

CASE 1.—Clinical Report: E. H., white, twenty-nine years of age, unmarried, entered the hospital Nov. 19, 1931, with the complaint of vaginal bleeding. An appendectomy and right salpingo-oophorectomy was done in 1926 and a tonsillectomy in 1928.

Menstruation began at seventeen, flow usually moderate, of about three days' duration, and not accompanied by pain. The interval between menses varied from four weeks to six weeks. The patient denied any pregnancies but admitted frequent coitus prior to May, 1931. She denied sexual intercourse after this date.

The last menstrual period which seemed normal to the patient occurred July 15, 1930. The patient stated that a physician who examined her subsequent to this time told her that she was not pregnant. Prolonged periods of bleeding with short irregular intervals of quiescence followed.

In November of 1930, the patient suddenly had a profuse hemorrhage, severe enough to make her very weak. From this time until July, 1931, there were irregular periods of amenorrhea varying in length from four to six weeks with intervening periods of profuse menorrhagia lasting as long as ten days. After the first part of July, 1931, the uterine bleeding became continuous.

In September, 1931, the patient visited a physician and a dilatation and curettage were done, but the menorrhagia continued. These curettings were not examined by a pathologist.

Examination of the patient in the hospital revealed the following: pallor, weakness, well-healed right rectus scar, tenderness over lower abdomen especially in midline, a marital vaginal outlet, a firm cervix of normal size, a small freely movable firm uterus, and palpably normal adnexa. Dilatation and curettage yielded abundant uterine tissue diagnosed histologically as hyperplasia of the endometrium. The blood showed 70 per cent hemoglobin, 3,380,000 erythrocytes, and 8,400 leucocytes. The patient was discharged Nov. 28, 1931, without an adequate explanation of the menorrhagia.

She was re-admitted Dec. 31, 1931, complaining again of vaginal bleeding. During the interval menorrhagia had been continuous, requiring the use of 24 pads weekly. The patient had been unable to work because of shortness of breath and weakness.

Examination now revealed marked pallor. There were tubular breath sounds at the right base. Marked presystolic and systolic murmurs could be heard over the precordia, and most distinctly over the aortic area. Blood pressure 100/70. Pulse rate 104. There was tenderness on deep pressure in both lower quadrants. The corpus uteri seemed to be of normal size but the cervix was enlarged and irregular. The adnexa were normal to palpation. A necrotic mass of tissue 2 to 3 cm. in diameter was removed from the cervical canal. Sections of this material were diagnosed typical chorionepithelioma.

On Jan. 2, 1932, the hemoglobin was 55 per cent (Sahli) and erythrocytes 2,560,000. On Jan. 4, 1932, the patient was given a transfusion of 425 c.c. of blood, following grouping of both patient and donor as well as establishing specific compatibility. Laparotomy was done Jan. 12, 1932, and the uterus, without adnexa, extirpated. Friedman's modification of the Aschheim-Zondek test, using a pre-operative urine specimen, was reported January 14 as "strongly positive."

On January 15, the patient's condition was such that another transfusion was indicated. Blood compatibility tests were again carefully performed and a donor of a homologous group (IV Moss) was employed. At 5:30 P.M., the major part of 550 c.c. of blood had been given when she complained of abdominal pain which increased in severity. The procedure was abruptly terminated. However, the abdominal pain continued, became cramplike, and was referred to the hips. Adrenalin gave temporary relief. Later in the evening, cyanosis and profuse diaphoresis developed. Stimulants failed. The pulse became "thready and weak," respirations were labored, cyanosis increased and death occurred at 11:30 P.M., Jan. 15, 1932.

Pathologic Examination of Uterus.—The uterus measured 8 cm. from the external os to the superior border of the fundus and 5 cm. in its greatest diameter which was 2 cm. above the external os. The external surface showed no gross evidence of neoplasm.

A sagittal section of the uterus (Fig. 1) revealed a hemorrhagic polypoid mass extruding from the posterosuperior wall down into the uterine cavity. The lower portion of the mass presented at the widely dilated external os. The mass was

roughly round with a diameter of 4 cm. The diameter of the external os was 1.5 cm. This hemorrhagic polypoid tumor blended into the myometrium; being separated from the lumen of the uterus by a definite covering of endometrium and a thin layer of myometrium. This surface layer was ulcerated at the extreme inferior portion of the mass. The remainder of the uterus appeared to be uninvolved by neoplasm.

Microscopic sections made from tissue taken deeply in the tumor nodule (Fig. 2) showed the typical malignant chorionepithelioma of Marchand² or of the chorio-

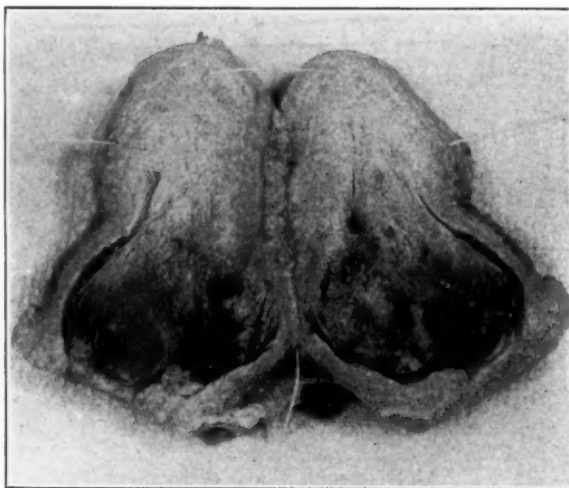


Fig. 1.—Case 1. A sagittal section of the uterus, revealing the hemorrhagic mass of chorionepithelioma extruding from the posterosuperior wall, everting the overlying myometrium and endometrium. Five-eighths natural size.

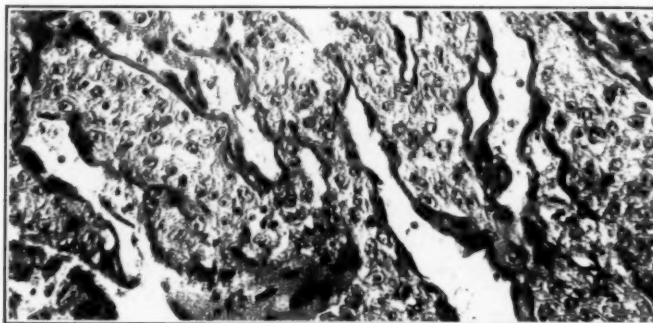


Fig. 2.—Case 1. A section of tissue taken deeply in the polypoid mass, showing typical chorionepithelioma. $\times 400$.

carcinoma of Ewing's classification.¹¹ Sections through the surface of the mass demonstrated an intact endometrial covering and a narrow zone of myometrium (Fig. 3).

Necropsy Report.—A complete postmortem examination was made Jan. 16, 1932. Nothing could be found to substantiate the clinical hypothesis that the final symptoms of the patient were caused by a transfusion with incompatible blood. *Staphylococcus pyogenes aureus* was cultured from blood removed from the right auricle. The gross and microscopic studies of the tissues confirmed the diagnosis of septicemia.

A small hemorrhagic firm nodule, measuring 1 by 0.7 by 0.8 cm. was situated

deeply in the parenchyma of the lower lobe of the right lung. Gray granular tissue was intermingled with the hemorrhagic material. This was the only remaining evidence of chorionepithelioma that could be found.

The left fallopian tube and ovary were present, but these structures were absent on the right. Corpora hemorrhagica or corpora lutea were not reported.

Microscopic study of the lesion in the lung (Fig. 4) revealed a mass of hyalinized fibrin and erythrocytes with intermingled tissue of placental origin. One distinct cross-section of a chorionic villus partially covered with a single layer of Langhans cells and a small mass of syncytium was present. Longitudinal sections of less definite bulbous chorionic villi were seen. A few small collections of Langhans and

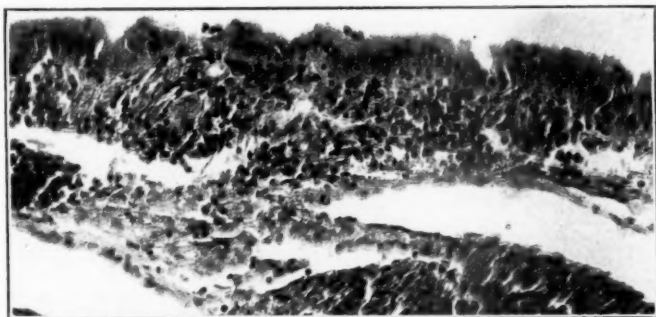


Fig. 3.—Case 1. A section through the surface of the polypoid mass, demonstrating the intact endometrium over the chorionepithelioma. $\times 400$.

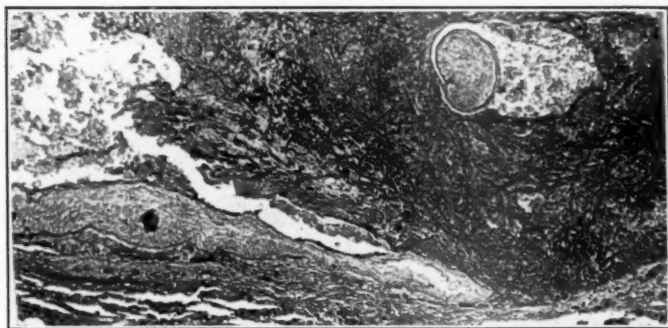


Fig. 4.—Case 1. Section of the hemorrhagic nodule in the lung. Note the embolic chorionic villus, cut in cross-section, surrounded by fibrin and erythrocytes. Observe the retrogressive appearance of its Langhans and syncytial cells. A villus, cut longitudinally, is present in the lower left of the field. Beneath it are partially collapsed pulmonary alveoli. $\times 80$.

syncytial cells, not attached to villi, were demonstrable in the fibrin and in the marginal lung parenchyma. The entire lesion appeared distinctly retrogressive.

CASE 2.—A. T., white, forty-two years of age, married, entered the hospital in April, 1932, complaining of hemorrhages from the vagina.

The menstrual history was not unusual. The first pregnancy was in 1918. It advanced to full term and resulted in a normal delivery. The second pregnancy terminated with the birth of a normal boy Nov. 12, 1926. This pregnancy was complicated by severe pyelitis, from which the patient gradually recovered following the delivery. The pyelitis recurred for a brief interval in 1928.

Menses remained normal and regular following the pregnancy in 1926, until Sept. 1, 1931, the date of the last menstruation that preceded a period of amenorrhea

which extended through September and October. At the end of October, the patient had a profuse hemorrhage which her doctor diagnosed as an abortion. The uterus was not curetted. Almost constant uterine bleeding, described as "a dirty discharge with a little old brown blood," occurred during the following five months. On April 1, 1932, she had another severe hemorrhage.

The patient was pale and weak. The uterus was tender and less movable than normal. The blood showed 4,000,000 erythrocytes and 75 per cent hemoglobin. Material removed from the uterus by curettage was reported as "no evidence of malignancy."

During an exploratory operation, as the uterus was being carefully manipulated, a very severe sudden hemorrhage occurred. The uterus was removed. In the lateral wall of the pelvis and involving the culdesac the surgeon observed what he described as "brown dead tissue, which could not be completely removed—part of the peritoneum and underlying cellular pelvic tissue, evidently necrotic."

Following the operation, the patient made a very satisfactory recovery. Several

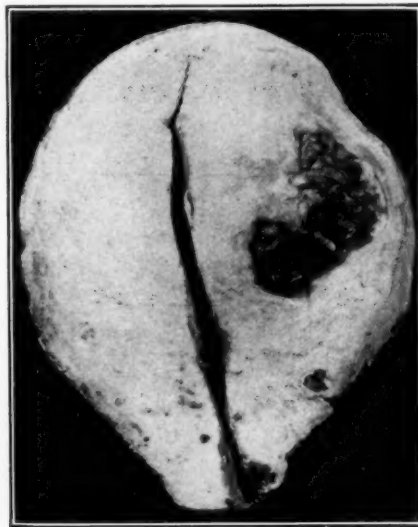


Fig. 5.—Case 2. A sagittal section of the uterus showing the nodules of chorion-epithelioma in the myometrium, separated from the normal uterine cavity by a thick layer of smooth muscle. Note the inaccessibility of the neoplasm to the curette. Natural size.

subsequent examinations were negative. Specimens of the patient's urine were submitted Jan. 24, 1934, and Feb. 9, 1934. Friedman's modification of the Aschheim-Zondek test resulted in a negative reaction with each of these specimens of urine.

Pathologic Examination of Uterus and Left Adnexa.—Around the left cornu of the uterus, extending into the broad ligament, was hemorrhagic appearing tissue which was not necrotic but was viable. The ovary measured 2.7 by 1.5 by 1.2 cm. It contained a corpus luteum 1.0 cm. in diameter. The uterus was globular, measuring 6.3 cm. superoinferiorly, 5.0 cm. anteroposteriorly, and 5.0 cm. laterally.

A sagittal section through the uterus (Fig. 5) showed the lumen to be of normal size, shape, and position, lined by smooth endometrium which showed no evidence of neoplasm. The anterior wall was 2.0 cm. thick and the posterior, 2.8 cm. A nodule of abnormal tissue, measuring 1.7 cm. anteroposteriorly and 2.8 cm. superoinferiorly, was situated in the posterior wall. This tissue was composed of thin-walled vesicle-like structures intermingled with grey granular tissue. The nodule, at its closest

point to the lumen, was separated from the endometrium by 0.6 cm. of myometrium. Extending from this nodule through the left uterine cornu into the broad ligament were small vesicles similar to those composing the main tumor mass. A smaller nodule of similar tissue, measuring 0.4 cm. in diameter, was situated in the lower uterine segment in the posterior wall, deeply in the myometrium.

Microscopic study of a section of the broad ligament near its attachment to the left cornu of the uterus revealed several thick-walled dilated veins filled with large bulbous, villous structures. The villi were ensheathed with a thick layer of Langhans and syncytial cells, the latter predominating. Fibrin, with intermingled erythrocytes and leucocytes, partially covered the surface. At some points, the villi were attached to the vessel wall, and, in a few places, the chorionic epithelium seemed to invade the wall. The remaining connective tissue of the broad ligament showed infiltration with fibrin, erythrocytes, and leucocytes, including many polymorphonuclear neutrophils.

A section of the hemorrhagic material deposited about the uterus and the broad ligament showed syncytial and Langhans cells and an occasional villous structure intermingled with fibrin, erythrocytes, and leucocytes.

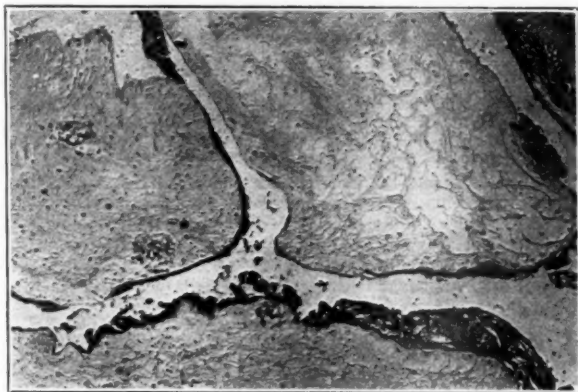


Fig. 6.—Case 2. Edematous chorionic villi, ensheathed by proliferating syncytial and Langhans cells, composing the nodules in the myometrium. $\times 80$.

A study of the histology of the nodule situated in the myometrium (Fig. 6) revealed edematous chorionic villi with sheaths of syncytial and Langhans cells. There was demonstrable invasion by chorionic epithelium of the surrounding smooth muscle. The adjacent myometrium showed acute inflammation and partial necrosis.

DISCUSSION

The histories of the two cases were similar in many respects. Both were white females of the menstrual age who sought medical attention because of excessive vaginal bleeding. The records indicated an initial period of pregnancy of about three months' duration for the first patient and quite definitely two months for the second. In each case, amenorrhea was terminated by a severe hemorrhage apparently the result of abortion. Careful investigation failed to reveal that material resembling mole was expelled by either patient. Irregular vaginal bleeding, intermittent in the first case, and remittent in the second, followed for fourteen and five months, respectively. Each patient

complained of discomfort in the lower abdomen. Palpation of the uterus elicited tenderness. Both showed definite clinical and laboratory signs of loss of blood. Uterine curettage failed to explain the menorrhagia of either patient, although late in the course of the first (after fourteen months), material extruded from the cervical canal was diagnosed chorionepithelioma. Hysterectomy was performed in both cases, and study of the uteri resulted in diagnoses of chorionepithelioma. The evidence was conclusive that the neoplasm found in each uterus originally had been encased in the myometrium, a sufficient distance from the endometrium to be inaccessible by curettage.

The mechanism of the development of chorionepithelioma in this site seems relatively obvious. Following the brief period of pregnancy, the endometrium rapidly extended over the placental site, entrapping bits of trophoderm located deeply in the myometrium. Such placental remnants are not uncommon.¹⁵ Usually they are rapidly absorbed, but they may lie dormant for long intervals, chorionic villi having been found in the uterine wall eighteen years after the last pregnancy.¹⁶ As chorionepithelioma has its origin from placental tissue, it seems fair to assume that entrapped portions of trophoderm might give rise to newgrowths at any time.¹⁷

The neoplasm initiated in the myometrium progresses along the lines of least resistance. If its location is near the lumen of the uterus, as the newgrowth increases in size, it tends to evert the mucosa and become a polypoid mass consisting of chorionepithelioma covered by endometrium and a thin layer of myometrium. Necrobiosis of the enveloping tissue leads to ulceration, and the neoplastic mass finally becomes accessible to the curette. Our first case illustrates this type of development. Should the newgrowth arise deeply in the wall, such eversion of the endometrium is not probable. The neoplastic tissue is now likely to extend along the vascular channels toward the broad ligament.¹⁸ Such a manifestation of the disease was present in our second case.

The literature revealed other cases of chorionepithelioma occurring in the myometrium in a position inaccessible to curettage.^{10, 11, 19, 20, 21, 22, 23} Some of these case reports described additional tumor tissue that was superficially available, but the accounts suggested that the primary neoplasm originated intramurally and probably remained in this location for some time, delaying a diagnosis based on the study of uterine curettings.

The morbid anatomy of the two neoplasms presented is not identical. The histopathology of the first is definitely that of the typical malignant chorionepithelioma of Marchand² or of the choriocarcinoma of Ewing's classification.¹¹ No one will question the very malignant appearance of this tumor. We also have made the diagnosis of "chorionepithelioma" in the second case. A tumor that has invaded the wall of the uterus, proliferated there, and extended along the uterine veins far into the broad ligament must be considered malignant.²⁴ We have not subdivided malignant placental neoplasms as Ewing¹¹ has recommended. However, it is our opinion that this tumor would qualify for his less malignant group, "chorio adenoma destruens." The present good health of the patient, in spite of the reported incomplete surgical removal of the neoplastic tissue and the demonstration of neoplasm in large veins, is in accord with Ewing's predictions for this type of case. The repeatedly negative Friedman tests obtained with the patient's urine indicate that viable placental neoplasm is not present in any of her tissues.

The reports of Sampson,¹² Ries,¹⁶ Mestitz,¹³ and Hansmann and Schenken¹⁴ indicate that the large vascular channels of the myometrium are quite accessible during normal pregnancy. Schmorl²⁵ and Dunger have found trophoblastic pulmonary

emboli in the lungs of women during pregnancy uncomplicated by placental neoplasm. If normal chorionic villi can erode vessels and become emboli to distant organs, it is not surprising that malignant neoplastic tissue derived from placenta should progress in a similar manner. The minute metastases, some of them in vessels, described in our two cases are examples of this mechanism of dissemination. Metastasis of chorionepithelioma by means of small emboli is probably the common method of extension to broad ligament, vagina, vulva, and lung.

The retrogressive appearance of the solitary metastatic lesion found in the lung of our first patient suggests rather interesting speculations. The histology of this lesion is in sharp contrast to that of the actively proliferating mass in the uterus. Two possible theories are offered. The lesion may be a true neoplastic metastasis, and, as such, an example of the pathology in the reported chorionepithelioma metastases that have disappeared following hysterectomy.^{10, 15} If this view is accepted, the case is an exception to Ewing's statement¹¹ that "there is no satisfactory evidence in the literature that metastases of tumors of this histologic type (choriocarcinoma) have ever spontaneously regressed."

Our second theory, and the one which we favor, assumes that the pulmonary lesion is the result of a nonneoplastic trophoblastic embolus of the type described by Schmorl.²⁵ An embolus of this nature, containing sufficiently viable cells to soften and rupture a vessel in which it lodged, could cause a pulmonary hemorrhage with consequent hemoptysis. If this occurred in a patient with a recognized chorionepithelioma of the uterus, the attending physician would be very likely to diagnose pulmonary metastasis and give his patient a more grave prognosis. If hysterectomy removed the chorionepithelioma, the patient might recover. In such an event, the clinician would probably interpret the case as a cure following hysterectomy for chorionepithelioma with metastasis. But, as we have indicated, the lung lesion would not be actually neoplastic.

SUMMARY

1. Two cases of chorionepithelioma have been presented in which the tumor apparently originated deeply in the myometrium. This location of the neoplasm made it inaccessible to the curette and consequently retarded the diagnosis.
2. The Aschheim-Zondek reaction or Friedman test should be an especially valuable aid to early diagnosis of chorionepithelioma of the intramural type.
3. Clinical symptoms suggesting chorionepithelioma, together with a strongly positive Aschheim-Zondek reaction or Friedman test, yet no evidence whatever of placenta or placental neoplasm in uterine curettements, should indicate surgical exploration. Such a procedure may often result in the early diagnosis and adequate treatment of an intramural newgrowth of placental origin.

4. A retrogressing hemorrhagic pulmonary lesion containing placental tissue has been described; and the disappearance of pulmonary metastases of chorionepithelioma has been discussed.

5. The probable mechanism of metastasis of chorionepithelioma has been explained.

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Von Szathmary: Brenner Tumors in the Walls of Ovarian Cysts, Arch. f. Gynäk. 154: 390, 1933.

The author reports five Brenner tumors all cystic in character, thus falling into the second group according to R. Meyer. This is unusual, since the second group is the smaller of the two groups into which this uncommon type of ovarian tumor can be classified. They are entirely different from granulosa cell tumors, since they are both histologically and clinically benign. They apparently have no effect upon the uterus; myomas are frequently found in association with them. These tumors definitely arise from the epithelial elements of Walthard's cell groups.

RALPH A. REIS.

McKinney, Stewart, and McClure: Suppurative Ovaritis Following Mumps, Lancet 2: 22, 1934.

There is only one other report of suppuration in the ovary in association with mumps. The patient ran a febrile course, developing a mass in the lower left iliac fossa. Twelve days later when vomiting began the abdominal cavity was drained. The left ovary was found necrotic, and only one-sixth of the right was conserved. A few adhesions involved the tubes. The uterus was retroverted. The appendix was normal.

Three weeks later the patient was discharged from the hospital in good condition.

H. CLOSE HESSELTINE.

ANALYTICAL STUDY OF CESAREAN SECTIONS IN A HOSPITAL SERVICE OF 9,000 DELIVERIES*

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WHAT are proper indications for cesarean section?" The answer to this question must be conditioned by adequate recognition of involved maternal and fetal morbidity and mortality. The operation was originally advised for the extraction of a baby whose life was of primary concern, but now we also expect to secure the mother against immediate or consequential damage. While the various operative procedures have been fairly well standardized, perfection in technic constitutes but one of many factors bearing upon morbidity and mortality. Why an operation of relatively easy performance should carry the highest reported morbidity and mortality of any uncomplicated pelvic-abdominal operation is not easy to understand. The reason must be less in the operation than in the failure properly to interpret or evaluate the attendant general and obstetric facts regarding the patient. Obstetric judgment is no less important than good obstetric therapy. They are inseparably necessary for satisfactory results.

Our purpose is to record the factors and results attendant upon the performance of cesarean section in a large maternity hospital during a two-year period among 9,000 deliveries. It serves as a basis for critical analysis of reasons and results, with consideration of other contingent data not given statistically. The aphorism that statistics speak the language of the analyst is negated by defining standards, as for the morbidity tables, and supplying incidental data which might have any influence upon those recorded.

INCIDENCE OF CESAREAN SECTION

There were 177 cesarean sections, representing 2 per cent of 8,852 deliveries in the Margaret Hague Maternity Hospital during a twenty-four-month period up to October, 1933. Thirty-three patients who aborted in the first trimester of pregnancy and 115 who miscarried in the second trimester are deducted from the 9,000 for quite obvious reasons.

Without analyzing at this time the indications for section, it must be noted that of the 177 operations performed, 26 were done on patients who had previously had cesarean sections. This does not mean that we blindly accept the conservative and generally sound dictum of "once a cesarean, always a cesarean." When a

*Presented before the Academy of Medicine of Northern New Jersey, Newark, N. J., November 2, 1933.

patient has previously had a low transverse laparotrachelotomy operation, without morbidity, and where the primary indication did not preclude the possibility of subsequent relatively easy vaginal delivery, a mild trial labor is permitted, and in our experience many such patients deliver spontaneously. There was no mortality in this group, although one ruptured uterus occurred. Of the 177 sections performed, 151 were upon patients not previously subjected to the operation.

Probably more important than resectioning patients is the occasion and incidence of cesarean section in women who have previously delivered, even with indifferent results, vaginally.

Fifty-six patients of the series had previously delivered vaginally, 31.6 per cent of the total. In their previous deliveries, of 28 patients with cephalopelvic disproportion, 17 or 60 per cent had delivered stillbirths. Of the others, 11 were sectioned because of placenta previa, 7 for cardionephritis and heart disease, 4 for abruptio placentae, 2 uterine tumors, and one each for brain tumor, tuberculosis, and stenosis following cervical amputation. These data are of importance, and yet they do not measure the persisting pelvic trauma still in evidence in many of this group, as a result of former obstetric experiences. Incidentally there were but 4 morbid cases among those sectioned after previous vaginal deliveries, a morbidity of 7 per cent.

INDICATIONS FOR OPERATION

The most frequent indication for section was contracted pelvis, totaling 100 or 56 per cent. Of these, 75 were generally contracted and 21 of the simple flat type. The next largest group, 26 in all, were patients who had previously been sectioned. The third largest group was composed of 15 cases of placenta previa, of which 9 were of the central type. Cardiac disease furnished the indication in 10 cases, and nephritis in 7.

Fibromyomatous uteri in 3, dystocia dystrophy syndrome in 2, and abruptio placentae in 5, and a scattering of 7 other indications with one case each.

In the resectioned cases *all* presented indications at the first operation which still militated against proper vaginal delivery. In this group, cephalopelvic disproportion rightfully assumed responsibility for 24 or 92 per cent of the total. It is evident that promiscuous use of the operation for varied indications is not existent.

EFFECT OF AGE AND PARITY

Age seems to have little effect on cesarean incidence. But if it is remembered that 55 per cent of the total operations were on primiparas and that while the vast majority of patients delivered during this two-year period were under thirty years of age, 40 per cent of these sectioned were over thirty, it is readily apparent that patients, especially primiparas beyond thirty years, have a distinctly greater chance of having pregnancy terminated by cesarean section.

RELATION OF OPERATIVE INDICATION TO MORTALITY AND MORBIDITY

Contracted pelvis was the most common indication, and here also was the highest morbidity rating, i.e., 14 or 14 per cent. The fetal mortality in this group was 7 or 7 per cent. The question arises whether in this most difficult group requiring the greatest judgment to handle, some of these patients were sectioned at a time and in a condition when they were not only more likely to influence morbidity rates, but were more apt to lose the baby as well.

Where patients had been previously sectioned, a total of 26, there were two instances of morbidity (7.7 per cent). There were no fetal deaths in this group. Thus

it appears that these patients protected from the hazards of a fruitless labor because of their previous experiences, have the happiest expectancy.

The placenta previa group shows the value of good judgment. Fifteen of 83 placenta previa patients delivered in two years were subjected to abdominal hysterotomy, an incidence of 1 to 5.5 (18 per cent). The results in this group were excellent, as there were no maternal deaths, and no morbidity. There were only 4 fetal deaths (only one beyond the eighth month of gestation), and 11 babies left the hospital in good condition. The operation in this group was reserved mainly for patients in whom vaginal delivery presented undue additional hazards, or for placenta previa with severe bleeding through an undilated cervix, especially in primiparas.

Ten patients with heart disease as the primary indication were operated upon, and one died within a day of cardiac failure. Her death was impending and the operation was undertaken mainly in the interest of the child, which survived. There was but one fetal death, and the results in this group of selected cardiac cases are considered satisfactory.

There was only one maternal death in 5 patients operated upon for abruptio placentae, and this proved to be uteroplacental apoplexy at operation. The fetal mortality was 100 per cent as would be expected. Only when maternal survival seemed incompatible with vaginal delivery was cesarean section resorted to in this group.

Only 2 patients were sectioned with preeclampsia as the primary indication and none for eclampsia. There was one fetal death (seven months, 790 gm. fetus, colored, ill nourished in a fibromyomatous uterus).

TYPE OF OPERATION

The operation chosen in 116 cases, or two-thirds of the total of 177, was the low cervical type laparotrachelotomy with the transverse incision popularized by Phaneuf. The DeLee or Hirst modification, through the lower segment and cervix, was done in 8 cases. Of the 35 classical sections done, 5 developed fever, as contrasted with a morbidity of 11 per cent in the laparotrachelotomy groups. Fifteen Latzko operations were performed in frankly or presumably infected cases, with no deaths, and 20 per cent morbidity. There were 5 deaths or 4.2 per cent in the Phaneuf operation, and two deaths or 5.7 per cent in 35 classical cesareans.

TYPE AND AMOUNT OF ANESTHESIA USED

One hundred and sixty-two of 177 patients had spinal anesthesia alone, and 7 spinal anesthesia with supplementary gas-ether. A majority of the spinal injections were performed by resident internes, and there were no anesthesia deaths. Three patients were given ether, and one died under the anesthetic. Four had local anesthesia alone and one avertin and local.

Primiparas having cesarean sections totaled 99 or 55 per cent of the total, the majority of the indications being cephalopelvic disproportion. Nearly all of the cases of nephritis and heart disease were in multiparas, while secundiparas and tertiparas claimed many of the group which should have had sections at first delivery or who had unexpected complications following previously normal vaginal delivery.

CONDITIONS AFFECTING MORBIDITY AND MORTALITY

It is apparent from Table I that it is quite safe to permit labor to proceed for a period up to twelve hours. It is likewise permissible to defer decision within twelve hours of rupture of the membranes. But following the "twelve-hour safe period," there is a rapid and precipitous climb in morbidity. It is not always possible to

apply this lesson to a given case, but the "twelve-hour safe period" should constantly occur to the obstetrician in considering factors bearing upon the manner of terminating pregnancy.

Vaginal examinations must not be done upon prospective section cases unless one is ready to accept a trebling of the morbidity rate. It is not our custom to make vaginal examinations; the rectum offers a digital check on labor progress. Vaginal examinations are reserved for cases where they seem clearly indicated or necessary and are made with the patient prepared as for delivery.

TABLE I. CONDITION AFFECTING MORBID AND FATAL CASES

I. Membranes ruptured:

HOURS	TOTAL	MORBID	PER CENT	FATAL	PER CENT
0-12	120	5	4.2	5	4.2
12-24	14	3	21.4	2	14.3
24-38	12	4	33.3		
48 or more	8	3	37.5		
Not determined	23	7	30.4		

II. Vaginal examinations:

NUMBER OF EXAMINATIONS	TOTAL CASES	MORBID	MORBIDITY PER CENT	FATAL
None or one	161	17	10.6	7
Two	13	4	30.8	
Three or more	3	1	33.3	

III. Hours in labor:

HOURS	CASES	MORBID	MORBIDITY PER CENT	FATAL
0-12	90	4	4.4	4
12-24	37	4	10.8	1
24-48	36	8	22.2	2
48 or over	14	6	42.9	

After proper preparation, one vaginal examination is made routinely before abdominal section. On rare occasions it had led to change in type of interference. Rectal examinations, if unskillfully done, may be positively dangerous in patients with ruptured membranes where a severe cervicitis existed during pregnancy.

Thus it may be briefly stated that for best operative results, the patient should not be examined vaginally and should be operated upon within the "twelve-hour safe period" as regards hours of labor and duration of ruptured membranes.

CAUSES OF MORBIDITY

The standard taken for morbidity was a rise in temperature of 100.4°, on any two days after the first day. Table II shows the causes, when determined. In one-third no cause for the temperature rise could be found, and the patients remained

TABLE II. CAUSES OF MORBIDITY

1. Pyelocystitis	6
2. Infected wounds	4
3. Peritonitis	1
4. Culdesac abscess	1
5. Myometritis	2
6. Vesical-abdominal fistula (Latzko)	1
7. Undetermined	7

asymptomatic and made uneventful recoveries. In only 9 of the 22 morbid cases could the temperature be directly traced to the operative field itself.

FETAL DEATHS

There occurred 21 fetal deaths, a mortality of 11.8 per cent. However, 4 of these were under seven months gestation, 5 were accompanied by abruptio placentae and dead before operation, and 2 were hydrocephalics which died shortly after birth. In 10 instances or 5.6 per cent were the deaths either unexpected or preventable.

MATERNAL DEATHS

Among the 7 fatal cases, four were unexpected, two from peritonitis, one from ether anesthesia, and one from embolism when the patient was ready to go home. In three patients, one in uremia, one in cardiac decompensation, and one with uteroplacental apoplexy and shock which refused to yield to the most energetic measures and repeated transfusions, the outcome was in accordance with the presenting condition. In the uremic and cardiac patients the operation was performed in the interests of the fetus, as maternal death was impending.

Seven deaths in 177 operations gives a mortality rate of 3.9 per cent, or in "corrected" terms, 2.2 per cent.

COMMENT

The greatest problem in dealing with patients with contracted pelvis is the management of those primiparas with "borderline" pelvises who rupture membranes before or very early in labor. When the pelvis is generally contracted and the disproportion obvious, the indication is clear. With the membranes intact, an adequate trial is available. But where there is moderate pelvic contraction, or a simple flat pelvis, with early rupture of the membranes, retarded cervical dilatation, and maladaptation of the head, the finest obstetric judgment is needed. The danger in these "borderline" cases is delaying operation until the mother is exhausted and an easy prey to complications, and the baby likely to succumb. Review of the data presented above, showing the past obstetric history and fetal deaths in patients who delivered vaginally at previous parturitions, and consideration of the very high maternal morbidity and fetal mortality (9.5 per cent) in flat pelvis, is convincing evidence of the accuracy of this belief. Unbelievable numbers of women must bear disabling testimony that their vaginal delivery was effected at a terrific price and with a staggering number of fetal deaths.

When patients have previously had cesarean sections, we believe resection advisable, with certain reservations. When the indication for operation does not conflict with possibly normal vaginal delivery, the transverse laparotrachelotomy operation used, and no morbidity traceable to the operative field, a carefully watched trial labor is in order in the subsequent pregnancy. It is no disgrace to section some patients and later deliver them vaginally if the initial indication was just.

The absence of any maternal deaths in 15 placenta previa patients is noteworthy. This is largely due to our prophylactic pre- and post-operative treatment for hemorrhage. By no means do we advise cesarean section as routine treatment for placenta previa. Where a physician lacks special obstetric ability, cesarean section may give better results but that physician has no moral right to handle such a case. Cesarean section should be reserved for selected cases where the judgment of the experienced obstetrician indicates it to be the safer method for the lives concerned.

Our experiences indicate the suitability of cesarean section in certain cases of heart disease and nephritis. These patients should invariably be sterilized if conditions are such that operation is warranted. The results are good. Where the patient's death is inevitable, as in two of our cases, the operation may be used to save the baby without materially hastening the mother's death. In semimoribund cases, it must be done before placental circulation is greatly embarrassed to be of any practical use.

We would comment upon the rarity, in this series, of preeclampsia and eclampsia as indications for section. There were no patients with eclampsia sectioned and only two patients with preeclampsia. Two others had been cleared of preeclamptic symptoms before being sectioned because of flat pelvis. Cesarean section is a highly fatal operation in patients with eclampsia and too dangerous to use, with rare exceptions, in untreated preeclampsia.

In our hands, laparotrachelotomy with transverse cervical segment incision performed under spinal anesthesia is the operation giving best results; lowest mortality and morbidity, fewest fetal deaths, and least number of postoperative symptoms and sequelae. Our experience in this two-year study corroborates that of several preceding years. The Latzko operation finds a definite field in frankly infected cases, with a reasonably low morbidity (20 per cent) and in our 15 cases, no deaths. It may be preferable where an unsuccessful attempt at vaginal delivery has been made. The low classical operation may be preferred by some for placenta previa, or where sterilization is to follow operation, in spite of its definitely higher mortality, morbidity, and dangers if another pregnancy should follow.

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WHEN TO OPERATE IN RUPTURED ECTOPIC GESTATION*

AN ANALYSIS OF 247 CASES

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IN THE "Report on Maternal Mortality in New York City"¹ for the three years 1930 to 1932 inclusive, published by the New York Academy of Medicine, 120 deaths due to ectopic gestation are cited. This group forms 5.9 per cent of the total of 2,041 deaths, a proportion of one to every 16, an astonishingly large number if the number of ectopics encountered is compared with the number of deliveries. From this report the death rate cannot be determined, but in a report by McDonald² of a collection of 6,626 cases, all of the patients who were operated upon showed a general mortality rate of 7 per cent. Of the 120 deaths in the Academy report, 91 patients were operated upon and nearly all had symptoms at least a week previously. More than 70 per cent died within five days, indicating, according to the report, "that the shock incident to operation was too great." It is evident, therefore, that reduction in mortality depends upon early diagnosis and proper management.

With these two thoughts in mind, we studied the patients on the service at St. Catherine's and Greenpoint Hospitals, Brooklyn. There are 247 cases in this series. One hundred and twenty have been previously analyzed by Charles A. Gordon.³ His analysis was conclusive in showing the importance of diagnosis. For the purpose of the record we have added the rest of our cases, numbering 127, noting the diagnostic features of the entire series.

The age of the patients varied from eighteen to forty-two years; 191 or 77 per cent were between the ages of twenty-four and thirty-five. Fifty-three patients had never been pregnant and the longest period of sterility was sixteen years; 73 patients had not been pregnant in five years or more; 194 had been pregnant at least once.

Among the 247 cases there were 8 deaths, a mortality of 3.2 per cent.

The total included primigravida, 53; primipara, 50; multipara, 144, with 2 children 63, 3 children 40, 4 to 11 children 41.

In an effort to determine what may predispose to ectopic gestation we found that 56 had marriage infection as determined by typical history; 112 had previous abortions with several curetted; 49 had dysmenorrhea (premarital); 36 had complicated labor previously; 58 had operations, pelvic and abdominal, as follows: 22 appendicectomy, 2 cholecystectomy, 12 operations for ectopic gestation, 1 suspension of uterus, 2 cholecystectomy and appendicectomy, 1 oophorectomy, 1 "operation on intestines," 1 operation for intestinal obstruction, 2 colpotomy, 1 Dudley operation, 1 operation for umbilical hernia, 6 salpingectomy, 5 laparotomy for sterility, 1 appendicectomy and operation for ectopic gestation.

*Read at a meeting of the Brooklyn Gynecological Society, October 5, 1934.

The location of the ectopic pregnancy was as follows: right 138, left 107, not stated 2.

	RUPTURED	TUBAL ABORTION	TOTAL
Ampulla	142	72	214
Isthmus	22	--	22
Interstitial	5	--	5
Tubal stump	3	--	3
Not stated	--	--	3
	172	72	247

Vaginal bleeding occurred in 229 cases, and it was marked in 42. As a rule, however, the bleeding appeared as repeated spottings. The average period of amenorrhea was six weeks, a delay of two weeks, but 46 cases missed no period at all. Spotting and pain, however, ushered in the symptoms in every one of these cases. The blood counts were of great assistance in diagnosis and were recorded as follows:

	CASES
White cells: More than 10,000	180
Highest W. B. C. 51,000	
Polys at least 80%	142
Highest polys 95%	
Red cells: Less than 4,000,000	152
Lowest R. B. C. 1,340,000	
Hemoglobin: 50 to 70%	151
Lowest hemoglobin 25%	
Sedimentation time: 18 to 210 minutes	
(60 cases, no constant findings)	

In tabulating the symptoms of which the patient complained we found that 247 had pelvic pain, 123 repeated syncope, 147 vomiting of rupture, 31 passed tissue, 43 painful defecation, 76 painful urination, 36 chill, and 14 had primary pain in shoulder.

In examination of the patient we have noted the following: *Physical Findings:* pelvic mass 197, abdominal mass as well 29, mass indefinite 28, mass not mentioned 10, enlarged uterus 165, soft cervix 121, pain on moving cervix 202, fluid wave 40, shifting dullness 53, breast signs 26, and highest temperature 100° F. 192.

Rigidity, distention, and rebound tenderness were noted in many instances. All three are valuable signs but unfortunately they are often of short duration. They rarely persist. This very fact is, however, of significance in differentiating the diagnosis of ectopic gestation. Rebound tenderness was most persistent, occurring in 25 per cent of our cases.

Preoperative diagnosis was correct in 221 cases or 90 per cent. In 10 cases the preoperative diagnosis was not recorded. Incorrect diagnoses in the remaining 16 cases were as follows: fibromyoma uteri 1, twisted ovarian cyst 1, hydrosalpinx 1, pelvic abscess 1, ovarian cyst 1, fibromyoma with chronic pelvic inflammation 1, post-abortual sepsis 1, and chronic pelvic inflammation 9.

The important features that are of great assistance to us in making an early diagnosis have been presented. However, if we are to reduce the mortality in ectopic gestation, the management of the case will demand both judgment and skill.

Immediate operation is generally considered the proper procedure in the management of ruptured ectopic gestation. To quote Litzenberg,⁴ "Even though there be collapse, shock, and alarming blood loss, an operation should be done as promptly as circumstances will

permit," and Schumann⁵ says, "All cases of extrauterine pregnancy should be subjected to operation as soon as practicable, regardless of the condition of the patient." Curtis,⁶ however, states, "If the patient is in profound shock, temporary delay of intervention is usually advisable." Polak⁷ did not favor immediate operation. In his last reference to this question regarding what he called "tragic" cases he stated, "The immediate indication is to combat the shock and control hemorrhage; in an experience of over 400 consecutive ectopics (with a mortality of 2.1 per cent) the writer has done but one immediate operation." It is to this principle, advocated by Polak, that we have adhered in the management of our cases.

For the purpose of discussing this phase of the subject we have divided our 247 cases into two groups as he did—the nontragic and the tragic cases. Of the former there were 167 cases. The problem as to when to operate did not present itself in this group. All these patients were in such a condition that in our judgment they could stand the shock of operation. Either they had had but very little blood loss or were in the reactive stage. They were operated upon after proper preparation.

In the tragic group there were 80 cases. All these patients came to us showing evidence of great blood loss. All were in shock, blood pressure was low, frequently it could not be recorded, and pulse was rapid and of poor quality, often imperceptible. The body surface in many of these patients was cold and clammy. The blood picture and clinical appearance of the patient, in every instance, indicated profuse hemorrhage.

It is with this latter group of 80 tragic cases that we are concerned in our discussion of when to operate. The problem would not have presented itself in the majority of these cases if diagnosis had been made when symptoms first appeared. In 59 instances there was a clear history of previous, and often repeated, rupture, and the average time elapsing before the patient entered the hospital after the rupture that produced the tragic picture was eighteen hours.

It was our judgment that patients in the tragic group were not fit to stand operation. We felt that the added shock incident to operation would be too great and our patients could not survive. With this as our problem our efforts were devoted to combating the shock.

The treatment at this time consisted of absolute rest, ward screen, shock position, complete morphine immobilization, one-fourth to one-half grain on admission, often a fourth within the hour and another fourth every three or four hours, external heat, no stimulation, no enema. We have found hypodermoclysis with Ringer's solution very valuable and, on account of its slow absorption, not at all contraindicated. Blood transfusion played an important rôle; however, in many instances this measure was not resorted to, improvement taking place

to our satisfaction without it. We feel that in spite of the most careful typing and cross matching of bloods, transfusion is not without risk. (One of our fatal cases we classified as a blood transfusion death.) This does not mean that this measure is not a valuable and life-saving procedure in the management of ruptured ectopic gestation, but it is not the panacea that some would have us believe, nor does it in any way guarantee a successful operation. More than 50 of our patients improved without it, so as to be satisfactory subjects for operation.

Notable reaction occurred usually within a few hours: our efforts were rewarded in 75 instances in the 80 cases. The improvement was such, that in our judgment, operation could be performed without undue risk to the patient. In 5 cases improvement was not noted. It is our policy to institute treatment to combat shock in all tragic cases. Blood pressure is frequently taken (the cuff constantly remaining on the arm), the pulse repeatedly recorded, frequent blood counts taken, and the general condition of the patient constantly observed. Failing to react, operation is performed anyhow. However, it is only in very rare instances that such an occasion arises.

When the patient has reacted to the point where she will in our judgment stand the operation, it is performed. Further delay has its dangers, too, in that rupture may again take place, and hemorrhage recur. Operating when the systolic blood pressure is between 90 and 110 has proved a safeguard for us against this catastrophe.

Operations were performed by 8 operators. The skill of the surgeon should be, and is, an influence when the decision as to when to operate is to be made. Crossen⁸ states: "In these cases immediate abdominal section is advisable as a rule, if the patient is within reach of an experienced abdominal surgeon and can be placed in suitable surroundings. In the absence of an experienced operator and suitable facilities, operation had best be deferred." It is obvious that the expert may, with comparative safety, operate upon patients in varying degrees of shock. However, the casual operator cannot expect good results in such cases. Many tragic cases will fall into the hands of the unskilled, and to our minds best results are to be obtained if shock is first combated.

That ruptured ectopic gestation calls for surgical intervention is clear. That operation should be done at once is generally held. It would seem that the patient is suffering from progressive hemorrhage, is bleeding to death, and the bleeding vessel must be ligated. That active bleeding is not often encountered at operation even in our most tragic cases is evident in our series. Only six times was it noted, and then it is reasonable to assume that pelvic exploration, or even opening of the abdomen itself, may have caused it. Halliburton and McDowall⁹ state: "Unless a large vessel is opened hemorrhage is for

various reasons seldom fatal. The damaged blood vessel retracts and contracts and this, together with the clotting of the blood, tends to close the opening while the formation of a clot is facilitated by the fall of arterial pressure. For these reasons, section even of such a large vessel as the radial artery may not cause death."

Seventy-six of the patients in our 80 tragic cases were operated upon and the operative procedures are noted in Table I.

TABLE I

REMOVAL OF	ALL CASES	TRAGIC CASES
One tube	140	53
One tube and ovary	91	23
Both tubes	6	0
Uterus	5	0
Ovum from tube and resuture	1	0
Appendix also	5	0
No operation	4	4

No anomalies were noted, although examination of torn and distorted material is very difficult.

The appendix was removed in 5 cases of the nontragic group. This certainly should not be done, nor should any other operative procedure accompany that which is done for ruptured ectopic, with the abdomen filled with blood.

In all but one tragic case correct diagnosis was made, and this without culdesac puncture; which we consider unnecessary and perhaps dangerous. All patients presented a large amount of blood in the abdominal cavity, and only the large clots were removed. There was no drainage in any case.

The location of the pregnancy was as follows: ampulla 52, isthmus 19, interstitial portion 4, fimbrial end 2, and not determined 3.

In this series of 247 cases there were 8 deaths, a mortality of 3.2 per cent. Briefly the details of these deaths were as follows:

1. In profound shock on admission. Had curettage for pain and bleeding two weeks before admission. Died six hours after admission. This patient failed to show any improvement whatever. Was never fit for operation. Autopsy showed extensive rupture in the isthmus.

2. Admitted with imperceptible pulse, blood pressure 0, cold and clammy skin. Died four hours later. Absolutely no improvement and never in condition to be operated upon. Had sought relief for pain, vomiting, and bleeding one week before, and condition diagnosed as threatened abortion by family physician. No operation, no autopsy, but included in this series because our diagnosis was ruptured ectopic gestation.

3. Died five minutes after admission. History of rupture eight hours before. Autopsy, rupture of interstitial portion of tube.

4. In shock on admission. Condition remained unchanged but operation was performed anyway, after delay of eighteen hours. Rupture of tube at isthmus. No active bleeding. Died eleven hours later. Death due to shock. Two days before admission attended by family physician, and again day before admission. Refused advice to enter hospital until what was probably a third rupture occurred.

5. Admitted with diagnosis of postabortal sepsis. Cured ten days before admission to induce abortion. Admission diagnosis of septic abortion made; not seen by attending staff. Expired three hours after admission.

6. In shock; responded to supportive treatment, operated upon and died twenty-four hours later of acute sepsis. Family physician prescribed for pain and bleeding two days before admission.

7. In shock on admission. Reacted to supportive treatment, operated upon, died twenty-four hours later of acute sepsis. History of rupture eighteen hours before admission.

8. Admitted in shock. Operation after reaction. Bleeding controlled. Blood transfusion given while patient was still on operating table following operation. After 180 c.c. were given sudden unexpected death. Clear history of rupture two days before admission.

From the above it will be noted that 5 patients did not improve under treatment. Only one was operated upon, and eleven hours later she died of shock. Of the patients who did not improve one was in the hospital only five minutes, one three hours, one four hours, and one eighteen hours. In this last case the fact that the patient was not improving was not appreciated. In one case the diagnosis was not made.

Of the patients that did improve, one died after a transfusion and two died of sepsis.

Four of these patients were not operated upon. In the 243 patients that were operated upon there were 4 deaths or an operative mortality of 1.7 per cent.

In all there was a definite history of rupture from eight hours to two weeks before admission and 5 of the 8 patients had been treated at home for symptoms indicating rupture.

SUMMARY

1. In this series of 247 cases of ruptured ectopic pregnancy diagnosis was not difficult; pain and bleeding were present at some time in every case.

2. Eighty cases or 32 per cent were in shock on admission, and operation was delayed. In all but 5 of these 80 cases shock was combated successfully, and 75 cases or 94 per cent improved sufficiently to withstand the added shock of operation.

3. The total mortality of 8 or 3.2 per cent might have been less if transfusion had always been as quickly obtained as it is today.

4. There is no evidence to show that this mortality would have been any lower if immediate operation had been done. On the contrary we feel that such a policy would have increased the risk for all these tragic cases.

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600 McDONOUGH STREET

THE MANAGEMENT OF PROLAPSE OF THE UTERUS*

WITH ESPECIAL REFERENCE TO THE MANCHESTER-FOTHERGILL OPERATION

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IN MAY, 1933, W. Fletcher Shaw presented to the American Gynecological Society a paper on "The Treatment of Prolapsus Uteri, with Special Reference to the Manchester Operation of Colporrhaphy." He reported 549 cases with 96.3 per cent free from recurrence, slight morbidity and no mortality; he sees no reason why anyone should do any other operation, or why prolapse should be divided into different types for various operations. For forty-five years, according to Shaw, this operation has been done by a large number of gynecologists in Manchester on all patients with prolapse, irrespective of age, social position, or parity, and "the results allow more nearly a guarantee of cures . . . than does any other operation in surgery." W. E. Fothergill, by whose name the operation is best known to us because of his very practical modification of Donald's original technic, has published equally good results. Alfred Gough in 300 Fothergill operations found it perfectly adequate in 95 per cent of his cases, so satisfactory that he hardly dared modify it; he states that this operation is practiced by a large proportion of British gynecologists.

At the same time this operation has not found favor here, although it is known to many, and particularly to those who have seen it done in Manchester. Maier and Thudium, however, have reported 138 cases with cure in 111 out of 113 followed up, or 98 per cent; of 47 in the childbearing age, 11 patients had 13 children, with 10 normal deliveries. In Fothergill's cases, 26 had 30 children subsequently, 27 normally, while in Shaw's series, 27 had children, 5 with recurrence of prolapse.

Anatomic discussions needlessly complicate the subject. No doubt there are many factors involved in maintenance of the uterus at its normal level in the pelvis; the structures of the pelvic outlet must be interdependent. Mackenrodt's description of the cervical attachment of the strong connective tissue sheaths of the uterine vessels has not been universally accepted, although the Manchester-Fothergill operation aims to shorten this supporting tissue. Bissel's investigations, according to Goff, have convinced him of the importance of the visceral portion of the endopelvic fascia beneath the uterine vessels in the bases of the broad ligaments, the so-called cardinal ligaments of the

*Read at a meeting of the Brooklyn Gynecological Society, October 5, 1934.

uterus; the posterior cervical part of this same fascia also aids, while the vesicovaginal fascia, he thinks, is areolar and too weak for much support. Nyulasy shows illustrations and Spalding photographs of these cardinal ligaments, yet Koster has not been able to find them. An important part of the Halban operation is the reefing of the very vesicovaginal fascia which Goff has found to be so frail; not dissectable as a distinct layer according to Goff, Spalding found it to be 1.5 cm. thick, and Halban maintains that it can be found and dissected free in every instance. It should be observed, however, that none of the gross dissections or microscopic studies of Spalding, Sears, Goff, or Koster was made on a patient with prolapse, whereas it is our experience that in such patients the transverse cervical ligaments are much lengthened and hypertrophied and contain muscular tissue which probably originated from the uterus. It is obvious, too, that no uterus could descend without elongation of the parametrial supporting tissue, whatever name we may give it, and there is no reason why compensatory hypertrophy may not follow great elongation of this tissue; in other words, its density may increase with the functional demands upon it.

That the peritoneal ligaments of the uterus are unfortunately named and of little value for support is obvious. The importance of the levator ani is a subject for discussion. Because we have seen great stretching of the vaginal tube with rolling out of its walls, deep forceps laceration of the lateral vaginal sulci, and because complete tears of the perineal body into the rectum are rarely associated with prolapse of uterus, and never cause it, we have felt that levator fascial repair was of little importance. Since we see severe lacerations without prolapse, and prolapse without lacerations, one cannot cause the other. We have rebuilt the posterior wall only to narrow the vagina, change its direction, lengthen it when possible and place beneath the uterus firm tissue which would at least make descent difficult and tedious. Rectocele precedes prolapse and has nothing to do with it.

At St. Catherine's Hospital the Department of Obstetrics and Gynecology has elected the Manchester-Fothergill operation for prolapse since 1917. Then we thought that hysterectomy was the worst operation one could do for prolapse, yet it is obvious that prolapse may be cured that way. The Mayo-Goffe operation was done only when intrinsic pathology warranted removal of the uterus. In no case was relief of prolapse attempted by abdominal operation alone. A combined operation has been done for associated intraabdominal lesions, and five of our early Fothergill operations, the last in 1928, were subjected to some form of intraabdominal shortening of the round ligaments. That was unnecessary. Interposition we have always thought limited in its application and of doubtful expediency. No other operations have been done.

We have reviewed 170 consecutive cases of prolapse of the uterus admitted to St. Catherine's Hospital from 1917 to 1933. No case is included where the cervix did not descend at least halfway down the vagina, and no case of cystocele without similar descent. Grouping cases according to the degree of prolapse would be valuable, but there is no generally accepted classification. To some "third degree" or "complete" means protrusion of the cervix, and we found many cases in our records were so designated. It is clear, however, that complete prolapse should refer only to protrusion of the entire uterus, so I have found it more practical and informative to divide the cases into (1) protrusion of the entire uterus, (2) protrusion of part of the uterus and (3) descent at least half down the vagina, without protrusion.

TABLE I. DEGREE OF PROTRUSION

AGE	ENTIRE UTERUS	PART OF UTERUS	NO PROTRUSION	TOTAL
20-30	—	2	8	10
30-40	6	16	30	52
40-50	6	21	30	57
50-60	14	16	9	39
60-70	8	1	—	9
70-80	2	1	—	3
	36	57	77	170

The fundus was absent in one case of protrusion of the cervix with complete inversion of the vagina. Enterocoele was recorded in only four cases, but I think that its recognition is not easy unless well established. Cystocele and rectocele occurred with prolapse in 142 cases; the absence of rectocele was noted in 28 cases. The fundus cannot descend without carrying the bladder with it, but the cervix, by hypertrophy of its supra- or infravaginal portion or both, may protrude with or without cystocele or rectocele, in one case without cystocele the long thin portio was found four inches beyond the vulva. Elongation of the cervix occurs very frequently with prolapse, but it also occurs without it. The cause of this lesion is unknown. Anatomically it is not prolapse, but clinically it is. Those cases listed as hypertrophy of the cervix with protrusion, and inversion of the vagina from above downward, not everted from below upward as in classical prolapse, are tabulated in Table II.

TABLE II. PROTRUSION OF LONG CERVIX

Without cystocele or rectocele	4
With cystocele only	12
With rectocele only	4

The obstetric history is interesting chiefly because in 121 cases, or 71 per cent, there had been no instrumental or operative delivery. Tabulations are shown in Table III.

The most common symptoms were urinary: urgency, frequency, incontinence, nocturia, tenesmus, burning and inability to void without replacing the prolapsed mass; discharge, menorrhagia, postmenstrual bleeding, bearing down, protrusion, pelvic pain, dysmenorrhea, rectal tenesmus and backache were other symptoms recorded. Backache is a classical symptom of prolapse, yet many women did not complain of it, and for that matter, some did not complain of protrusion either, although it was

TABLE III. OBSTETRIC HISTORY

Spontaneous		121
No. of children	{ 1 only	12
	{ 2-14	109
Instrumental		40
No. of children	{ 1 only	10
	{ 2-7, first instrumental	9
	{ 2-7, one or more instrumental	10
	{ 2-11, all instrumental	11
Not stated		9

considerable. There is no constant symptom, and symptoms are of no importance as aids to diagnosis; they should be recorded, however, as complaints for which the patient seeks relief.

TABLE IV. OPERATIONS FOR PROLAPSE

Watkin's interposition	4
Mayo-Goffe vaginal hysterectomy	14
Manchester-Fothergill	152
Manchester-Fothergill with round ligament operations	5
Manchester-Fothergill with other procedures	14
	170

The Watkins operation was done four times, all on patients in the fifth decade. Large cystocele was the indication. The last operation was done in 1929. The Mayo-Goffe operation was done 14 times. The youngest patient was forty-one, the oldest sixty-seven. In the two cases before the menopause, the hysterectomy was done for adenomyosis in one case, dysmenorrhea in the other. In the other 12 cases, hysterectomy was done for postmenopausal bleeding (8), possible malignancy of the cervix (3), and fibroid (1). In no case was malignancy found by the pathologist. One patient had a pulmonary embolism. All recovered.

The Manchester-Fothergill operation was performed in 152 cases, in 50 of these without amputation of the cervix. So far as possible we have cauterized or occasionally repaired the cervix of young women because we fear that amputation may later cause abortion. In no case, however, have we left a measured uterine depth of more than three inches. In all cases high posterior colporrhaphy was done. Description of the operative technic is unnecessary, as we have modified Fothergill's very little, taking care only to use Halban's sphincter stitches in patients with urinary incontinence. Interrupted chromic gut No. 2 was used throughout, with No. 1 for subcuticular skin closure. Diagnostic curettage was not done routinely. Denudations were as wide as possible and then trimmed, as it is best to overcorrect vaginal slack. Preoperative preparation consists of rest in bed until ulcers and swelling are relieved; obviously it is safer to await healing of cervical ulcers, but where time presses the actual cautery may be used at operation. Postoperative care is simple; no douches, occasional gentle irrigations with boric acid solution with a glass catheter and a syringe, glycerin enema on the fourth day.

Other operative procedures were combined with vaginal plastic surgery in 19 cases; hemorrhoidectomy (1), intrauterine insertion of radium (2), vaginal myomectomy (1), abdominal myomectomy (1), appendectomy (2), inguinal hernioplasty (1),

appendicectomy and cholecystectomy (1), salpingo-oophorectomy (2), shortening of round ligaments (5), and supracervical hysterectomy (3). The last three cases need further explanation. One was for a large myoma, and the other two for bleeding associated with pelvic pain. In every case a heavy ring of cervical tissue was preserved at the level of the internal os.

It will be observed that, except for the occasional incidence of fibroid or adenomyosis, patients with prolapse are singularly free from other pelvic pathology. In no case was malignancy of the corpus present. Cancer of the cervix was not found by the pathologist in the four cases in which its presence was suspected; these cases had vaginal hysterectomy without previous biopsy. In one plastic, however, with amputation of the cervix, a diagnosis of cervical carcinoma was made on the tissue, and radium was placed in the cervical stump twelve days later; this patient has remained well three years without recurrence. Chronic pelvic inflammation, so common otherwise, was not seen nor was its presence suspected in any case. Diabetes was present in four cases. Many patients were not good risks, and a few early operations were done in two stages. No one was rejected for age. One patient with complete prolapse, myositis ossificans and ankylosis of both hips was satisfactorily operated upon although the approach was difficult.

Anesthesia was gas-oxygen-ether or ethylene in 158 cases; two were done under spinal novocaine, and in 10 cases, 8 Fothergill and 2 Mayo, local anesthesia was used, injecting first the perineum and labia, then the sulci and parametria; the anterior wall itself rarely required infiltration. Of late years all patients are given 9 gr. of luminal or 10 gr. of veronal with $\frac{1}{4}$ gr. of morphine or $\frac{1}{150}$ gr. of scopolamine before operation. This preliminary medication is essential to the success of local anesthesia, which is now routine for all cases and perfectly satisfactory. Now poor risks are not rejected.

MORTALITY AND MORBIDITY

There were two deaths in this series, one from bacteremia ten days after the vaginal plastic, the other from pelvic thrombophlebitis. This last was a two-stage operation. Although the record is not clear, I suspect that peritoneal sepsis followed repair of enterocele. This 1 per cent mortality is high for vaginal plastic surgery. Although Shaw has reported 549 cases with no deaths, he has had nine deaths in twenty-six years. We should expect no mortality from the Fothergill operation.

Slight bleeding about the sixth or seventh day is not uncommon after the Fothergill operation, nor is foul discharge. Two patients bled severely on the sixth day and one was lightly packed; this was probably due to infection and sloughing. Eight cases were complicated by pelvic cellulitis with the peritoneal rebound and low abdominal tenderness of parametritis. Two had phlebitis. Two had pulmonary embolism, one after Mayo, the other after Fothergill; both recovered. One had psychosis, another a strangulated hemorrhoid due to a suture, and another cellulitis of the arm due to hypodermic injection. No other complications were recorded. All the other patients recovered nicely, and were allowed out of bed on the fourteenth day.

END-RESULTS

All these operations were performed by four operators. In 94 cases follow-up has been sufficiently close and personal to warrant a report on the end-results of the Manchester-Fothergill operation, since all of these were private patients operated upon by me and observed at intervals for at least two years, many for three years and some for as long as thirteen years.

In every case prolapse of the uterus was cured and the uterus found at a level high enough to cause no symptoms of bearing down or weight. However, one patient, aged forty-nine, with a history of seven operations for prolapse over a period of thirty years, complained, within six months, of recurrence of all her symptoms of dragging, pelvic pain on standing or walking, urinary frequency and vaginal fullness; cystocele had recurred, but the cervix was high and fixed with dense scar tissue about it. In two cases large enterocele recurred within three months of operation; repair was satisfactory. In three cases cervical stricture caused hematometra, relieved by dilatation. It had not been our practice to thoroughly dilate the cervical canal at the time of operation, as advised by Shaw and Fothergill; this should prevent this complication. In nine cases urinary symptoms still persisted; in none of these, however, was secondary anterior wall repair thought necessary, although in six cases moderate cystocele was present. If we consider urinary symptoms, slight cystocele and hematometra minor defects, and enterocele or large cystocele evidence of failure, 91 cases were satisfactory results or 96.8 per cent.

In this group of 94 patients, 22 were in the childbearing age. Four have had one baby since the operation, and two have been delivered twice; in one of these when the rigid cervix was cut, delivery was prompt and spontaneous; her next delivery was easy. In all these cases the perineum was cut or torn, but prolapse did not recur. One patient had two abortions, each in the third month, doubtless due to amputation of the cervix.

CONCLUSION

It has been clearly shown by many operators that even the worst types of prolapse of the uterus may be cured by vaginal plastic surgery. No abdominal operation then should be done for prolapse. Since the parametria may be united in the midline without removal of the uterus, why remove it? Hysterectomy should be reserved for those patients in whom the uterus is diseased; removal of the normal uterus for the cure of prolapse is unnecessary, and in young women wrong. The Manchester-Fothergill is all that could be desired, and it should have no mortality. That it does not interfere with parturition may not perhaps be proved, but many women have been successfully and easily delivered after operation. Reviewing our results after

seventeen years' experience with this operation, we are satisfied that it accomplishes the most with the least risk, and that has always been a good rule in surgery.

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TWO YEARS' EXPERIENCE WITH THEELIN TREATMENT OF GONORRHEAL VAGINITIS*

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TREATMENT of gonorrheal vaginitis by the use of female sex hormones first suggested by Dr. Robert M. Lewis¹ opened up an interesting new field in therapeutics, namely, the use of hormones to alter tissues in such a way as to combat infection.

In a recent study, Jungblut and Engle² attempted to reproduce in immature monkeys a state of mature insusceptibility to the virus of poliomyelitis. They showed that immature monkeys prepared with glandular anterior pituitary hormones and anterior pituitary-like principles from the urine of pregnant women are protected only in exceptional instances against intercerebral infection with poliomyelitis virus. However, the serum of such prepared animals frequently acquires the property of inactivating the virus in vitro.

Lewis quite properly approached the subject of this hormone treatment conservatively, cautioning against possible dangers of the treatment, and subsequent articles by Brown³ and by Haberman and Israeloff⁴ have also been encouraging but cautious. The apparent simplicity of this treatment and its favorable preliminary reports might, however, lead to the hasty conclusion that a lasting cure is easily obtained.

Fundamental questions present themselves: (1) Does arrest or cure take place and, if so, how often and how permanently? (2) Are there any deleterious effects on the children?

*Read at a meeting of the New York Obstetrical Society, October 9, 1934.

NOTE: For lack of space the extended tabulations of cases could not be included. These may be found in the author's reprints.

The answer to the first question cannot be made in a definite manner, as yet, nor can we answer the second question except to say that, so far, no bad effects have been noted. It seems desirable, therefore, to present further experience with this treatment and to caution that it is still in the experimental stage.

The present series of sixty-eight cases was studied in the Hartford Municipal Hospital, and its Out-Patient Department, with the exception of the last five, whose records were furnished by the courtesy of Dr. Louis F. Middlebrook who has studied them at the Hartford Dispensary. This latter clinic has also cooperated in part of the care of many of our other patients.

With the exception of the first few cases the hormones used have been purchased in the open market. The necessity for economy in spending the city's money has led us perhaps to underdosage as will be seen in reviewing the protocol summaries. The hormones used were Parke, Davis & Co.'s theelin and theelin in oil, given intramuscularly, and theelol capsules, by mouth, G. W. Carnrick Co.'s thelestrin, intramuscularly, E. R. Squibb & Sons' amniotin in oil, given by mouth. (Where amniotin is mentioned in the protocol the oral product is indicated.)

In order to obtain a bird's-eye view of the effect of treatment from week to week, a special chart was used. We have used the well-known gradation of 1-4, in which 4 is the largest amount observed and 1 is the smallest, 0 being absent. Such a system is, of course, not absolutely quantitative, but in a general way, if done by the same observer, it is better than the use of descriptive terms.

We have estimated the amount of vulvovaginal irritation, discharge, and the intensity of the theelin reaction, as described by Lewis. All smears were taken with a wire loop, using the knee-chest position in the older children. We have noted the amount of vaginal material obtained and its appearance before drying as it is spread on the slide, for we have noticed that when squamous cells were numerous the fresh smear has a translucent or glassy appearance as contrasted to the muddy or opaque appearance when white blood cells are numerous.

On the microscopic examination we have noted the presence of intracellular or extracellular organisms, Gram stain being used throughout, and have tried to estimate the relative number of white blood cells and squamous cells.

The bacteriologic work was done in the Hartford Board of Health laboratory as part of its routine work, and it is too much to expect that these quantitative estimates can be taken too seriously. We believe, however, that the careful study of the smear can replace the vaginal wall biopsy as a control of the theelin reaction.

Eight mothers of 12 children were known to have had active gonorrhea, seventeen of the children had one or more sisters who were infected, and in 3 instances, at least, contact infection from a sister seems to have been highly probable. In the absence of cultural studies, however, we can question whether every case was a true gonococcal infection, for upper respiratory infections and the exanthemes seemed to complicate the onset, or to bring about relapses after a child had been bacteriologically free for as long as six months.

Many complicating diseases occurred during the treatment of these children. Ophthalmia was seen twice and was treated independently, having apparently no effect on the vaginal infection. Proctitis was found once and was quickly cured following potassium permanganate rectal irrigations.

Urethritis was seen 6 times, usually in cases which tended to recur repeatedly. This complication, undoubtedly, was present for a time in others. The urethra apparently is uninfluenced by the hormone, for the reaction, especially in the negro children, can be seen to limit itself quite distinctly to the muellerian tissue, ending at the hymen. No local treatment was attempted for urethritis. Perhaps a ketogenic diet rendering the urine acid would be as effective as anything.

Salpingitis was seen only once in a young child, aged five, and twice in older children aged ten and eleven years, respectively. This infection regressed rapidly under simple bed rest.

Puberty reactions were observed in 3 children at ages nine, ten and eleven years, some months after treatment. These children were of Irish, Swedish, and German parentage, respectively. Swelling of the breasts was not observed in any of the younger children even under prolonged treatment.

A few of the cases, it will be noted, remained negative following treatment which seems to have been obviously insufficient, but we are reporting every case irrespective of the results. We feel that other defense mechanisms than the hormones have been at work, and it may well be that all we can do with the hormone reaction is to clear the vagina and keep it clear while the natural immunity reactions develop and while infections in the urethra clear up independently.

It was noted that fresh infections required much longer treatment than did old infections, again emphasizing the part that immunity may play.

A few interesting cases are given in more detail, as follows:

CASE 1.—E. S., admitted at age of six months with congenital syphilis and gonorrheal vaginitis. She was hospitalized as an orphan for nearly three years and left for adoption apparently cured of both diseases, in spite of many months of serious complications including otitis and bronchopneumonia. This child started theelin treatment as reported by Dr. Lewis, receiving 50 R. U. daily for fifteen days. A

relapse was treated again similarly with a total of 2,050 R. U. The smears became negative and have remained so for fifteen months when last examined.

CASE 2.—M. S., aged five years, admitted with lobar pneumonia and gonorrheal vaginitis. During her admission for pneumonia she was treated with the usual antiseptics and discharged after 10 negative smears only to have the vaginitis recur in three months. As reported by Dr. Lewis she was given 50 theelin R. U. for fifteen days. The vaginitis cleared promptly and the patient has been entirely negative except for a few extracellular organisms two and four months after treatment. Observed twenty-three months at last examination.

CASE 3.—M. Y. This patient was aged four days when first admitted as a feeding case. She was discharged and readmitted at age of three months with gonorrheal vaginitis, receiving local antiseptic treatments. At a third admission for recurrence she was treated with antiseptics for five months without results, and as reported by Dr. Lewis, theelin was then given, 50 R. U. for fifteen days. The vaginitis promptly cleared and she remained negative for two years. She was fifteen months of age when treatment was started. Unfortunately she showed a positive smear at her last examination, and we may fairly ask (1) whether this is a true recurrence, (2) whether it is a new gonorrhea, or (3) whether it is an infection simulating gonorrhea. Such cases show that the word "cure" must be discarded, and we must be more exacting in our follow-up requirements.

CASE 4.—M. B., an orphan, aged three years, acquired gonorrheal vaginitis evidently from her sister. She had been negative on daily smears three months previously when examined as a contact. This patient had one of the most extensive and persistent infections which we have seen, involving not only the vagina but urethra and rectum, with many condylomas surrounding the vulva and anus. She did, however, escape salpingitis. The child was studied also by biopsies and received theelin, 50 R. U. daily, or twice 25 R. U. Later theelol by mouth was tried, 50 R. U. with fairly good reactions. Amniotin in oil, 30 R. U. 3 times daily, by mouth, was tried for fifty-two days without noticeable effect. Thelestrin, at first, gave good reaction in doses of 25 R. U. twice daily, but a later shipment failed to give a good reaction in twice that dosage. She has always responded quickly with an intense vaginal proliferation when enough rat units were supplied. We are now trying to keep up a moderate reaction for three months to see if we can wear out the infection. The proctitis was treated by permanganate irrigations and cleared quickly. To summarize her treatment which has now lasted twenty-three months, she has had 20 series of hormone injections and 14 times has shown a more or less vigorous vaginal reaction. She has never shown tenderness of the breasts, and has developed into a sturdy, apparently healthy child, but the end is not yet in sight for she has just shown one more recurrence while under treatment.

CASE 5.—P. D., aged eight years, admitted with otitis media and gonorrheal vaginitis. She was started on amniotin in oil, by mouth, 30 R. U. twice daily, later increasing to 60 R. U. twice daily, and when no reaction was obtained we increased to 300 R. U. twice daily. A total of 19,230 R. U. was given, of which 12,900 R. U. had been recently standardized for us by Edgar Allen of Yale University. The three biopsies of the vaginal wall at weekly intervals showed no appreciable change during this oral administration and her smears remained positive. Under three series of injections of thelestrin, 50 R. U. daily, totaling 600, 400, and 600 R. U., respectively, the infection cleared up and she remained negative for five months when last seen. During June of this year, two months after stopping treatment, I noted beginning swelling of the breasts, and during July a well-developed "theelin reaction" of the vagina was seen, although no treatment had been given for over two

months, and she had shown the usual involution of vaginal epithelium subsequent to her last treatment. She is now nine and one-half years old, and it is possible that this reaction constitutes the first sign of approaching puberty. Whether or not it was hastened by the treatment remains a question.

CASE 6.—H. R., aged four years, admitted for gonorrheal vaginitis and started on theelol, by mouth, 25 R. U. 3 times daily. Three biopsies were taken at weekly intervals and showed a moderate reaction. Smears became negative after 3,175 R. U. were given but were positive again within a month. The second series of theelol, totaling 1,000 R. U., was given with a better reaction but prompt recurrence of the infection. A third series of 1,000 R. U. was given, 50 units twice daily, likewise a fourth series of 700 R. U. Theelin was then given hypodermically, 25 R. U. twice daily, totaling 1,350 R. U. A fifth series of 600 R. U. of thelestrin was given, and a sixth series of 550 R. U. was given. A seventh series of 1,800 R. U. of theelin in oil was given hypodermically, 300 R. U. daily, and an eighth series of the same dosage was given. Gonococci were last seen in the smear preceding the last series in June, 1934, and we are trying here also to keep up a vigorous reaction over several months, since this child relapses easily if treatment is intermittent.

Perhaps as an anticlimax we may mention the case "L. C.," a newborn baby delivered in another hospital of a mother who had gonorrhea. The child quickly developed a gonorrheal ophthalmia and vaginitis and was started on theelin, 25 units twice daily for 22 doses before being admitted to the Municipal Hospital. She was under constant observation in our clinic until, at the age of four months, she left town. This child, beginning at the tenth day of life, had almost constant daily injections of 50 units, receiving in all 3,250 R. U. The theelin reaction of the vagina was constantly present but pus cells and the gonococcus did not disappear in the smears during three and one-half months of treatment. Fortunately, we were able to have this child brought back for follow-up examination just one year after birth, at which time she was clinically and bacteriologically free from any sign of infection. It is only fair to state that the theelin treatment may have had a beneficial effect, though it is disappointing not to have seen the infection clear up while under treatment. Clinical improvement, however, was marked, and we had expected the gonococci to disappear in a short time of additional treatment when the child was removed from our care.

CONCLUSIONS

1. Gonorrheal vaginitis may be cleared up more or less promptly in many cases following the establishment of a female sex hormone reaction, as described by Lewis.
2. Relapses are frequently due to reinfection from the urethra, and will be found more frequently if long-continued follow-up studies are made.
3. Acute recent infections require longer treatment and larger doses than long-standing infections.
4. One of the first signs of approaching puberty appears to be a vaginal epithelial proliferation which cannot be distinguished from the hormone reaction described by Lewis.
5. We have gained the impression that the vaginal infection, whether it is due to a gonococcus or other organism, responds equally well to the treatment.

6. We suggest tentatively as a plan of treatment that the child be cleared as rapidly as possible with daily injections of at least 100 R. U., preferably in divided doses, diminishing the amount as a reaction is obtained but maintaining a vigorous squamous cell reaction until the gonococcus disappears, and thereafter maintaining over a period of two or three months a moderately well-developed reaction, during which time the child may be allowed to go to school, subject to weekly observation by smears.*

7. We cannot say that this treatment is harmless, for we do not know what it is doing to the ovaries, and we await with curiosity the opportunity to inspect the ovaries at operation. So far, at least, deleterious effects have not been manifest.†

8. We have presented a study of female sex hormone treatment of 68 cases of gonorrheal vaginitis of which 42 have been observed for six months or longer. Twenty-three of these have been observed for one year or longer.

9. End-results of these 42 cases may be given in terms of negative smears for the time stated, and in which the result apparently had some relationship to the treatment, as follows: Good results, 19; temporary control only (up to the present time), 16; frank failures, either due to insufficiency of dosage or lack of cooperation, 7; 26 cases studied less than six months are not included in this summary. Further subdivided, the results may be given as follows:

Over one year:		Six months to one year:	
Good	6	Good	13
Temporary	12	Temporary	4
Unsatisfactory	5	Unsatisfactory	2

We wish to express our thanks to Dr. Robert M. Lewis for allowing us to participate in this interesting research, and for his many helpful suggestions during the course of the study.

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*An excellent study of the social significance of gonorrheal vaginitis as it affects the schools is contributed by Ella Oppenheimer and Roy H. Everett in the J. Social Hyg. 22: 129, 1934.

†Recently this opportunity presented itself during an operation for appendicitis on a nine-year-old child who had received 50 units of thelestrin twice daily for ten days. Vaginal clippings showed a typical Lewis reaction. Biopsy of the ovary showed no reaction.

CESAREAN SECTION AND ITS ABUSES*

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IN THE past decade we have witnessed a great increase in the incidence of cesarean section in this country. Unfortunately this rise in the number of operative deliveries has not been accompanied by a corresponding decline in mortality, either maternal or fetal, but on the contrary, by a higher death rate. Truly a sad state of affairs. A questionnaire sent to hospitals in this country by the White House Conference brought to light incidences of cesarean section as high as 14.6 per cent in some hospitals. Plass found the incidence in the southwestern states to be highest when compared with other sections of the country. It is worthy of note that although one sees great differences in the incidence of cesarean section in foreign clinics, one fails to observe there the excessively high rates as seen in some of our American institutions.

We would not be so concerned over the incidence of cesarean section were it not for the fact that this operation, as done throughout the country, carries with it a maternal mortality close to 10 per cent. Large series of cases have been reported from different sections of the country, carrying with them maternal mortality rates ranging from 1.7 to 16.1 per cent. In 1927 Davis reported a figure for this city of 14.4 per cent.

It needs no argument on my part to convince you that such results cannot and should not be tolerated. At last the lay public is waking up and asking our profession: Why this sacrifice in mothers? This steadily increasing tendency to effect delivery by operative means, mainly on the part of the improperly trained and unskilled, but sometimes also on the part of those who should and do know better, has been a great factor in keeping our maternal mortality rate in the neighborhood of 7 to 9 per 1,000 live births. The improvement that may be effected in a few scattered areas is more than offset by this ever rising tide of unnecessary operative deliveries with their frightful death rates.

Plass in his excellent statistical study of this question stated that a conservative estimate of the maternal death rate in cesarean section in this country is between 5 and 10 per cent and probably nearer

*Read before the Post Graduate Medical Assembly of South Texas, Houston, Texas, October 3, 1934.

the latter figure. He estimated that 25,000 cesarean sections are done each year in this country, which would mean a death list of 2,500 mothers a year. Three-fourths of these sections are undoubtedly unnecessary, in other words close to 2,000 women are unnecessarily sacrificed each year due to this urge to operate. I agree with Plass when he states that "a diminished cesarean section incidence would result in bringing our national maternal death rate down more nearly to that of other countries where vaginal delivery is more common and where the physiologic character of labor is better appreciated."

I shall present the statistics on cesarean section for the Woman's Clinic of the New York Hospital. They cover a period of two years, from Sept. 1, 1932, when the hospital was opened, up to the present time. During that period we had 5,456 deliveries in the hospital with 153 cesarean sections, an incidence of 2.8 per cent. Of these 153 women one died, the cause of death being a postpartum hemorrhage.

There were 11 stillborn or deadborn babies, due to the following causes:

Premature separation	5
Intrapartum infection	3
Ruptured uterus	2
Asphyxia	1
Total	11

From Table I it will be seen that the classical section is first, with the low cervical second in frequency. Rarely do we perform vaginal section and almost equally rarely the Latzko.

TABLE I

TYPE OF SECTION	PREMATURE	FULL TERM	TOTAL	% TOTAL
Classical	4	71	75	49.020
Low cervical	1	39	40	26.144
Radical		4	4	2.614
Classical or cervical + sterilization	4	25	29	18.954
Vaginal	1		1	0.654
Latzko		4	4	2.614
Total	10	143	153	100.000

In Table II are given the indications for 153 sections. Indications for cesarean section must be justifiable and the operation must be done at the proper time. If these two requisites are adhered to, what a difference there will be in this country in the incidence of cesarean section and in the maternal mortality rate incident to this operation. The operation of cesarean section is abused not only in respect to incidence, which means faulty and unjustifiable indications, but also in respect to the time of operation. An elective cesarean section should carry with it no maternal mortality. A section done late in labor, done long after rupture of the membranes and done after attempts at other

TABLE II. INDICATIONS

	TOTAL	% TOTAL
Contracted pelvis	80	52.28
Previous section (defective scar)	13	8.50
Premature separation	7	4.58
Placenta previa centralis	2	1.31
Chronic nephritis	13	8.50
Chronic valvular heart disease	10	6.55
Ruptured uterus	2	1.31
Fulminating preeclampsia	3	1.97
Cervical dystocia	6	3.92
Tuberculosis (renal)	1	0.65
Trial of labor (no progress)	3	1.97
Tetanic uterus	1	0.65
Previous myomectomy	1	0.65
Ovarian cyst causing dystocia	1	0.65
Prolonged labor with potential infection *	2	1.31
Transverse presentation	1	0.65
Disproportion between fetal head and pelvic inlet	1	0.65
Previous stillbirth	1	0.65
Hydrocephalus of infant	1	0.65
Old pelvic fracture with rupture of bladder	1	0.65
Large infant (breech)	1	0.65
Toxic myocarditis and preeclampsia	1	0.65
Face presentation, chin posterior	1	0.65
Total	153	100.00

types of delivery, carries with it an appalling maternal mortality. Should it become necessary to perform a section after hours of labor, it is imperative that some other type such as a low cervical, or extra-peritoneal operation be done.

In the exhaustive study of maternal mortality in New York City carried out by the New York Academy of Medicine Committee on Public Health Relations, it was clearly brought out what an important rôle the abuse of cesarean section plays in the production of a maternal mortality rate of about 6 per 1,000 live births for that city. Every obstetrician should study that Committee's published report. In it we read: "The incidence of cesarean section in the hospitals of the city is seen to be high—2.2 per cent of all deliveries, while it preceded almost a fifth of all deaths (19.8 per cent). This extremely high incidence in the series is a matter of concern. The indications as given on the records include some, such as toxemia, which some authorities no longer regard as valid. Slight degrees of pelvic contraction, in many instances, do not preclude delivery by the normal route, while malpresentation should rarely make a cesarean section necessary. Dystocia, prolonged labor, and similar terms are not definite ones, and doubt must be expressed as to the propriety of many of the operations undertaken for these reasons.

"More serious and closely related to the indications is the question of the choice of operation and the time of its performance. There is little doubt that in these two elements the greatest danger lies.

"The indications for the cesarean operation need re-statement and further limitation to really valid causes, such as severe degrees of contraction of the pelvis. More careful observation during the prenatal period should provide the opportunity for making a proper prognosis of labor and delivery, and so eliminate the use of the cesarean section as a last resort. The use of the classical type should be limited to the elective operation. The provision of the most highly trained specialist for every woman whose labor shows any abnormality will prevent the use of the cesarean section

when less dangerous methods of delivery could be used by those having the requisite training and skill. Sharp reduction in the number of cesarean sections performed is to be strongly recommended. Where the operation is required, only those whose training in abdominal surgery is adequate to insure proper performance of the operation should be considered suitable operators. Only by this definite narrowing of its use to the legitimate occasion demanding it, as well as the provision of capable operators, can a decrease in these deaths be achieved."

We do the classical operation in cases of elective cesarean section, that is, before the onset of labor and rupture of the membranes. I can see no reason for performing the low cervical operation in elective cases. The lower uterine segment is not very well defined and thinned out prior to the onset of labor; the low cervical operation being, therefore, more difficult and many of these actually result in a modified low classical section. The results in classical cesarean section performed at an elective time before labor gives excellent results.

In order that all of our sections be justifiable on indication grounds, and that most, if not all, be performed at an elective time, because it is in the group of elective sections that our results are the best, it is essential that we study our patients carefully during the last months of gestation in order that we may recognize, before the patient goes into labor, the necessity of operative interference. It is only in the group of elective sections, that we are sure of no ascending infection in the uterus at the time of operation.

Finally, I wish to stress that it takes more knowledge to know and more courage to heed the contraindications to cesarean section. Infection, demonstrable as well as potential, must ever remain before us a danger signal in any contemplated cesarean operation. Those who do not heed it, assume the responsibility of a life. Even with the perfected technic of the extraperitoneal and cervical operations, it becomes a serious undertaking to operate in the face of infection. Cases of this kind are brought to our attention constantly and we cannot make this warning too strong.

Cesarean section has a place in our obstetric armamentarium. Many lives have been, and will continue to be saved, by this operation. Unfortunately, due to the fault of our own profession, this operation, in its abuse, has caused the death of many women. It is clearly our responsibility, as physicians, general practitioners, as well as specialists, to correct this wrong. Let us place this life-saving operation in its proper setting, both in regard to indications, and in respect to time and skill of operation, in order that its abuse may become a legendary affair and our maternal mortality rate within the narrow limits of minimum.

PRELIMINARY REPORT ON STERILIZATION OF WOMEN BY INTRAUTERINE COAGULATION OF TUBAL ORIFICES*

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THE sterilization of subnormal women to protect racial integrity is regarded much more important by eugenicists than sterilization of the male. However, the necessity for an abdominal operation or the expense involved, especially in cases where no other operative procedure is indicated or the patient is a poor surgical risk, has been a serious handicap. If, therefore, it were possible to sterilize women in a simple office procedure, it would be of great therapeutic and eugenic value.

The first office procedure in sterilization of women was performed by Dr. Robert L. Dickinson.† By using a semiflexible electric cautery electrode, he was able to produce a burn at the site of the tubal opening of the cornua. The resulting scar tissue frequently blocked the tubal opening. After a period of sixty days the patency of tubes was tested by the Rubin method. Other operators have used chemicals for this purpose. But so far none of the methods have gained the wide use that the importance of the procedure would seem to warrant.

It was, therefore, believed that a coagulating current might be used in the same manner as the cautery and that it would be a safe procedure. A small group of the staff of the Mothers Health Clinic, Miami, Drs. Louise DeVore, Homer Pearson, M. C. Wilson, Buist Litterer, and Lydia Allen DeVilbiss began a series of cases.

The Florida laws contain no reference to contraception or sterilization. However under the Florida law a married woman cannot give legal consent. A release from responsibility similar to that used in hospitals was prepared by a legal firm to be signed by both husband and wife and witnessed. Coagulation of the tubal orifices is always referred to as "treatment." The patients are told that the treatment would probably make the woman less likely to become pregnant and it might prevent pregnancy altogether. After the first year when a number of cases had proved apparently successful, applications for the "treatment," were numerous, many of whom had to be refused because of their youth and lack of therapeutic or eugenic reason.

Coagulation of the tubal orifices requires no anesthesia, being practically painless. Occasionally the patient would speak of a cramping

*Presented at the Annual Meeting of the Eugenics Association, New York, June 4, 1934.

†J. A. M. A. 92: 373, 1929.

pain but there was no complaint. The patient is accepted for treatment after the menstrual period and is cautioned to come before she has had sexual relations.

METHOD

The patient is placed on the table and properly insulated. Under surgical technic a semiflexible uterine electrode is placed in the cornua and a current of varying amperage (approximately 3,500 milliamperes) is applied for fifteen seconds. In the first few patients the current was applied for not more than ten seconds. In these patients the tubes remained patent. The whole procedure, from the time the patient is placed on the table, does not require more than five minutes.

The patient is given a temporary contraceptive to use for the ensuing sixty days when she is requested to come for a Rubin test without having had relations following her menstrual period. This test consists of pumping air into the uterus under measured pressure. In the absence of a Rubin outfit, a surgical house supplied the attachments for an ordinary blood pressure apparatus. If the uterus holds an air pressure of from 150 to 200 mm. for from three to five seconds, the tubes are reported as blocked and the patient considered sterile. When the instrument indicates that air has passed into the tubes or the patient complains of pain under the shoulders within twenty-four hours, she has been given a second treatment and in a few instances even a third without any appreciable ill-effects.

RESULTS

The series of 30 coagulation cases was begun in January, 1933. Two of the 8 women of normal intelligence were premenopausal sterilizations.

At the first summary, January, 1934, 20 patients were reported with tubes blocked, 6 tubes patent, 3 no Rubin test, and 1 not treated.

Rechecking all cases as of January, 1935, 17 cases were reported blocked, 9 patent, 3 no test, and 1 no treatment. Seven patients had become pregnant, 3 of whom had been reported blocked, 1 partial blocked, and 3 no test. Two women have moved from the city. Twenty-two are reported nonpregnant, some of whom are using contraceptives.

CASE HISTORIES OF 7 FAILURES, (JANUARY, 1935)

CASE 14.—White paralytic moron, husband when drunk kicked her about. Reported blocked. She returned to the clinic pregnant, with signs of an impending abortion at about the sixth week and was sent to the City Hospital. The staff surgeons recommended a hysterectomy. The report of the pathologist follows:

Gross Pathology.—Amputated uterus 100 mm. by 70 mm. pale reddish yellow. Cut surface showed a pregnancy in left cornua. The endometrium throughout showed marked thickening with the exception of the area in the right cornua. In this area the surface was flattened and perfectly smooth. Wall of uterus 22 mm. in width.

Microscopic Pathology.—Section taken through area in right cornua showed almost complete absence of the epithelial covering with the exception of one place. There were no uterine glands present and the remaining muscle tissue was normal in appearance.

CASE 7.—Colored syphilitic moron, aged twenty-four. Married nine years, 5 pregnancies, 4 living children and 1 dead. Hemorrhage and temperature followed treatment. No Rubin test. No contraceptive or precautions used. Reported four months pregnant.

CASE 20.—White woman, aged thirty-eight, normal intelligence; married eighteen years, 8 pregnancies. Six living children and 2 abortions. Following the coagulation treatment the patient used no precautions against pregnancy and having reported her menses as normal was given a Rubin test sixty days after the treatment. Following the Rubin test she aborted. Subsequently fitted with a diaphragm pessary.

CASE 6.—White syphilitic moron, aged twenty-nine. Married ten years, 3 living children and 2 abortions. Hemorrhage and temperature followed treatment. Rubin test not advised. Given contraceptive which she did not use. Became pregnant and aborted. Fitted with diaphragm pessary which patient is not using but no subsequent pregnancies.

CASE 13.—White moron, aged twenty-seven. Six living children. Following the first treatment the patient's tubes were reported patent. The second treatment was reported blocked. The patient became pregnant and resorted to a criminal abortion. She then began using sheaths. Becoming pregnant again, she had a second criminal abortion performed. In this patient the floor of the perineum is so badly torn that a fitted pessary is not practicable so the patient is using sheaths with lactic acid jelly.

CASE 19.—White, normal intelligence, aged thirty-three. Eight pregnancies, 4 living children, 1 dead, and 3 abortions. Following the first treatment the tubes were reported patent. Following the second treatment the tubes were reported blocked. Using no precautions the patient became pregnant. Referred to a surgeon who, because of her serious physical condition, performed a therapeutic abortion, and a vasectomy on the husband.

CASE 22.—White, cardiac, aged twenty, normal intelligence. Three living children. Following the first treatment the tubes of the patient were reported partially blocked. Patient was given a diaphragm pessary and lactic acid jelly. The patient reported that on one occasion on removal of the pessary she found a good-sized hole in it. She claims this resulted in pregnancy. A previous physician reported that nothing he could recommend would keep this patient from becoming pregnant. Following this delivery surgical sterilization is recommended.

CONCLUSIONS

Intrauterine coagulation of tubal orifices is contraindicated in untreated syphilis because of the liability to hemorrhage. It must also be used cautiously in cases of gonorrhea since the blocking of tubes may interfere with tubal drainage, although this infection in itself likely will render the woman sterile. The resulting irritation from the coagulation current may also light up an old infection temporarily. Two such cases occurred in this series. The patients suffered pain and temperature for several days, however without any serious after-effects.

There is no positive assurance that the blocking of tubes with the coagulation method will be permanent. The longest a patient of this series has been under observation is two years.

The intrauterine cautery or coagulation method of sterilization may be recommended where surgery is inadvisable or contraindicated.

ABDOMINAL CIRCULATION DURING LATE PREGNANCY AS SHOWN IN AORTOGRAMS*

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SEVERAL years ago the Portuguese physicians, Egaz Moñiz and Dos Santos, astounded the medical world with their work on intra-arterial injections of roentgen opaque substances as a means of establishing the diagnosis of brain tumors and obscure intraabdominal conditions. This method at first was and still is considered audacious, and only few clinics have dared to confirm its value.

In the Urologic Clinic of our hospital we promptly adopted it and since 1930 have employed it frequently (Bisquertt,¹ Coutts,² Cantin,³ etc.) as a means of diagnosis in obscure renal and intraabdominal syndromes.

Conversant with the technic of aortic puncture, we decided to study through injection of the arterial system, the conditions of abdominal organs during the later stages of pregnancy. Twelve normal pregnant women, all over eight months, were submitted to this examination, which from our previous experience we knew to be harmless. Unfortunately one of these women died from meningeal hemorrhage following lumbar puncture.

The technic employed in all cases was as follows: Careful preliminary examination of the patient, especially as regards blood pressure since the intraaortic injection must be performed under spinal anesthesia. Patients with advanced arterial sclerosis are in our opinion unfit subjects for this method, although Bisquertt has obtained successful aortograms in cases of abdominal aortic atheroma and aneurysms. Renal and cardiac diseases, if not very advanced, are no contraindications.

The day before the injection we administer a mild purge and in the morning shortly before taking the aortogram, an enema.

When spinal anesthesia is complete, the patient is turned on the abdomen and her back painted once again with iodine. Four fingerbreadths to left of the spinous processes and anywhere between the first and third lumbar vertebrae, a medium caliber needle from 14 to 15 cm. long is pushed through the mass of spinal muscles until it comes in contact with a vertebral body. The higher up the puncture is made the greater are the chances to inject the celiac axis. The needle is then passed along the surface of the vertebral body. In pregnant women, once the needle has lost contact with the vertebra, it must be slightly tilted to the left, as the aorta has become partially displaced. At this moment the pointed stillette of the needle

*This paper, contrary to our custom of not accepting contributions from foreign sources, is presented because of the unusual character of the daring experiments made by the authors and their findings.

is withdrawn and the needle pushed forward with increased force in order to penetrate the arterial wall. In some cases, when the displacement of the aorta is not very considerable, it can be penetrated either by continuing the introduction in the original axis or giving the needle a slight inclination to the right.

If we have been successful in the search for the aorta, at the moment of puncture, a red, pulsating stream of blood flows through the needle. Blood flow must now be carefully watched for a few moments in order to ascertain its continuity; without this precaution we may fail to appreciate that the puncture has been incomplete, and when the opaque solution under these conditions is injected it will not enter the aortic lumen, but collect around this blood vessel.

As roentgen opaque fluid we utilize a 75 to 100 per cent solution of sodium iodide. This solution must be injected under pressure of one atmosphere. In order to obtain satisfactory aortograms we found that from 15 to 25 c.c. of the solution are

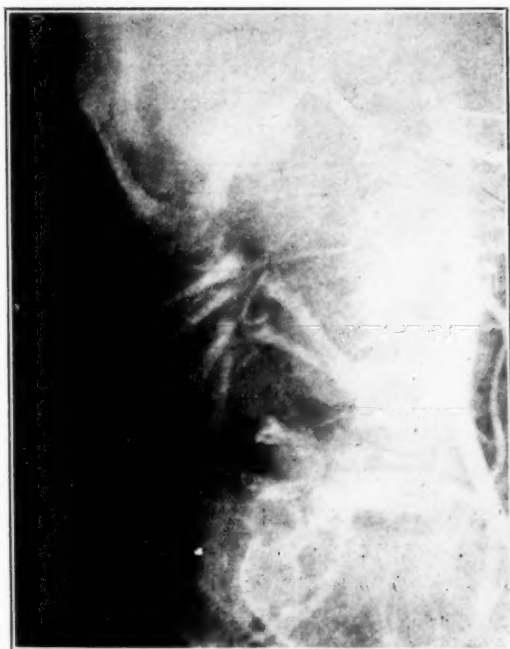


Fig. 1.

required, but if moderately tight rubber bandages are applied around the upper part of both thighs, thus retarding diffusion through the blood stream, 20 c.c. will prove quite sufficient.

Roentgenograms must be taken immediately after injection into the aorta is completed, and the time of exposure must be almost instantaneous. As soon as the radiogram is taken the rubber bandages should be removed.

The immediate effects of the injection are pains in the lower extremities and principally in the feet. Pulse becomes accelerated and soft, but is easily and quickly restored with the use of ordinary stimulants. If the sodium iodide solution should be distributed around the aorta, the patient will experience slight backache for a few days after the accident.

We performed our aortic injections in pregnant women selected from the Clinical Maternity by Dr. Sanhueza Donoso. All fetuses

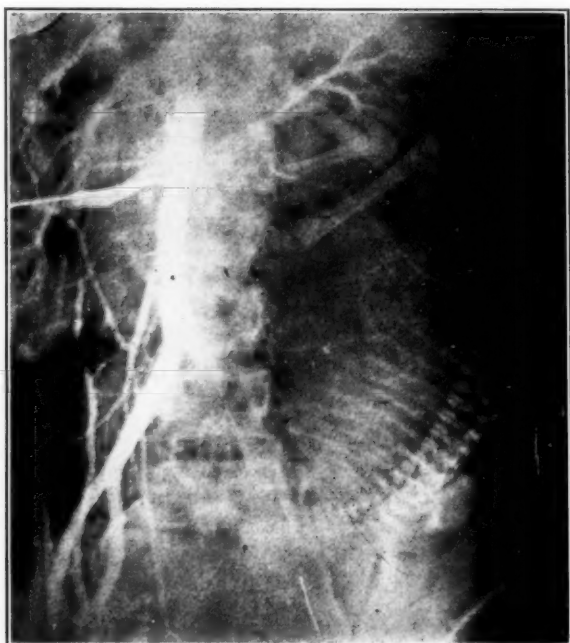


Fig. 2.

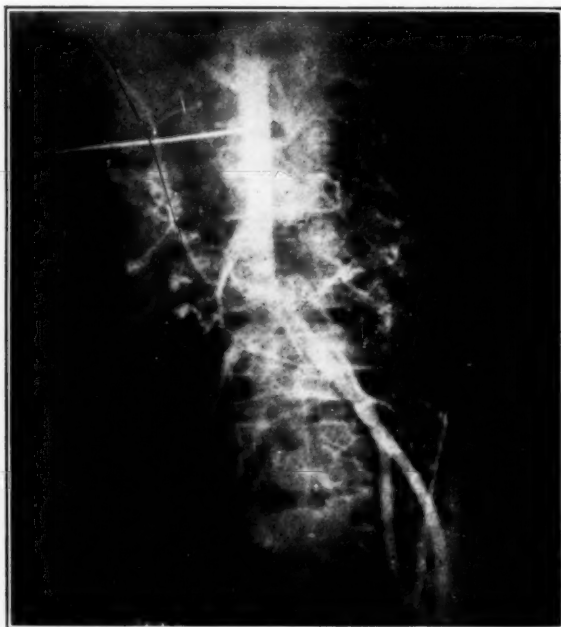


Fig. 3.

were carefully controlled before and after the injection through frequent recording of heartbeats; no changes could be detected resulting from the procedure.

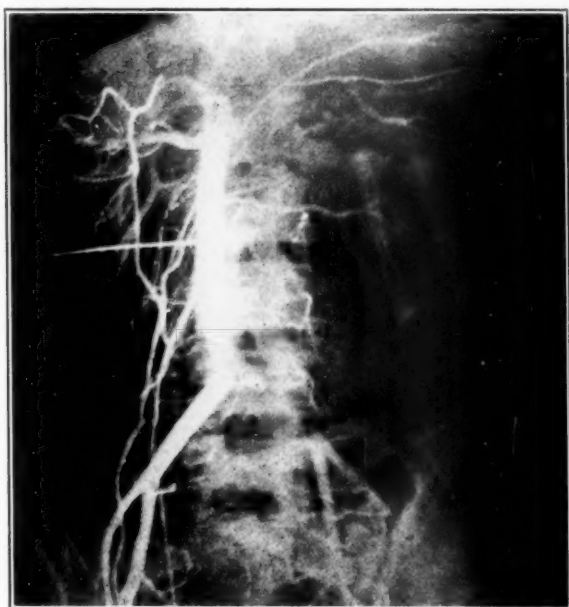


Fig. 4.



Fig. 5.

Study of the aortograms taken by us always shows varying degrees of aortic displacements to the left. In Figs. 1, 2, 3, and 4 the renal arteries run in an upward direction, proving that the kidneys are

pushed up by the pregnant uterus. This probably leads to a stretching of the ureters, which under such conditions could be more easily compressed by the distended uterus. Against this supposition, it might be argued that the renal displacement is due solely to the position in which the patient lies while the aortogram is made; this, however, is as well the position more or less maintained during sleep. We then would have to admit that during certain hours of the day this upward pressure on the kidneys possibly does not exist or acts less intensely than during the night.

In Figs. 1, 2, 3, and 5* definite filling defects in one or other of the common iliac arteries can be noticed. This defect stands in no rela-

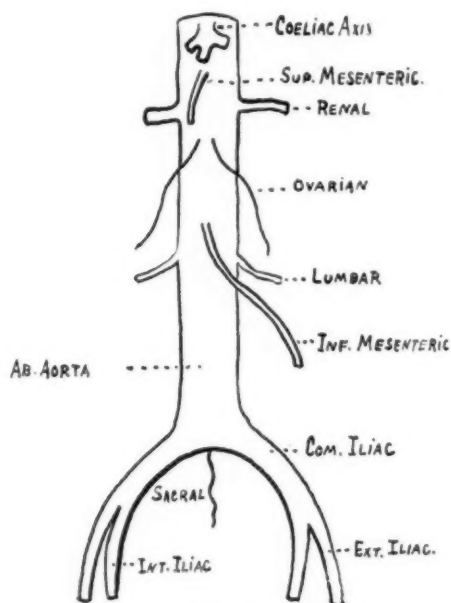


Fig. 6.

tion to the position of the head as can be ascertained by comparing the various illustrations. At first we attributed this phenomenon to pressure against the artery exerted by the pregnant uterus on account of the ventral position in which the patient was placed during the aortogram. Lately we proved through sphygmometric measurements that women in advanced pregnancy show marked differences in blood pressure in the two lower extremities.

The question arises whether this apparent deficiency in the arterial circulation of one side, as demonstrated by aortogram and sphygmometric records, does not result from the drainage of larger quantities of blood on this side through the uterine artery into the placental circulation.

*The horizontal lines in all the cuts indicate the needle penetrating the aortic wall.

Another fact we wish to point out is the apparent deficient arterial circulation observed in the areas supplied by the colic and sigmoid arteries on the left side. Deficient blood supply for these regions may lead to localized dehydration of intestinal contents and thus account for common constipation in pregnant women. It may also contribute to lower the natural defenses against bacterial absorption, especially of colon bacilli.

In Figs. 1 and 3 we can observe the injection of some placental sinuses; and in Fig. 3 certain vascular structures appear which apparently do not correspond to the maternal circulation and which we, therefore, believe to belong to the fetal circulation. Personally we feel certain that some of them belong to the allantoic arteries.

This modest contribution containing our findings and personal interpretation of ascertained arterial distribution of the abdominal aorta during late pregnancy and symptoms in relation with the changes noted, we present in the hope that it may serve as a basis for investigations and observations of others.

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DISPROPORTION AT THE PELVIC OUTLET INCIDENT TO FORCEPS DELIVERY

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GR^EAT resistance to forceps traction is frequently met at the pelvic outlet. Insuperable obstruction is not always avoidable even with a rigid exclusion of all cases of disproportion. Difficulties are still encountered after the correction of malpositions, and after an accurate biparietal adjustment of the blades, with the application of traction along the proper axis of the birth passage. Repeated failures after careful attention is given to all the technical details, and after all the classical conditions for forceps have apparently been fulfilled, lead one to suspect that not all the factors responsible for failure have hitherto been taken into consideration.

FETAL MORTALITY INCIDENT TO FORCEPS DELIVERY IN FUNNEL Pelves

Abundant statistical evidence is available to show that there is a high fetal mortality associated with forceps delivery in funnel pelves.

A study by Burgess,¹ of the results of delivery in contracted pelves, is particularly enlightening. This author presents an analysis of 106 operative deliveries in a series

of 389 cases of funnel pelves. There were 20 fetal deaths in the operative cases, an incidence of 19 per cent. Seventy-three of the operative cases were forceps deliveries. The fetal mortality incident to the forceps deliveries is not given separately, but is undoubtedly considerably higher than the average of 19 per cent for the series.

Similar results are reported by Duncan.² This author presents a series of 11 midforceps deliveries among 113 cases of funnel pelves. The fetal mortality in this group of forceps deliveries was 18.1 per cent.

In the San Joaquin General Hospital there were 87 cases of funnel pelves among the last 2,500 deliveries. The classification of funnel pelves was made according to Williams.³ In this group of funnel pelves there were 11 midforceps deliveries, 5 of which resulted in stillbirths. There was one pubiotomy, one version, and one craniotomy after failure with forceps. There were also 3 cervical cesarean sections after a test of labor and 6 elective sections.

There was no serious preexistent disproportion in the 14 cases in which midforceps delivery was attempted. This is attested by the fact that delivery occurred spontaneously in the remaining 64 cases with similar pelvic measurements.

For purposes of comparison, the midforceps deliveries in normal pelves were also reviewed. There were 34 such cases, and among these there were 5 fetal deaths, a mortality only one-third high as that obtained in the group of funnel pelves.

From the foregoing data, it seems that the obstruction encountered and the resulting failures are due not to preexistent disproportion, but to disproportion inherent in, and peculiar to forceps delivery in funnel pelves.

DEFLEXION INCIDENT TO FORCEPS DELIVERY AS A CAUSE OF DISPROPORTION

In funnel pelves, the head usually undergoes slight deflexion when it reaches the midplane. As it approaches the outlet, flexion is gradually reestablished, and finally becomes acute. In consequence of hyperflexion, a segment of the occiput, much narrower than the biparietal diameter, passes between the tuberosities.

In forceps delivery this process of adaptation fails to occur, and flexion remains imperfect. This radical departure from the normal mechanism is due to the circumstance that forceps traction must necessarily be applied along the mentooccipital diameter (instead of the cervicovertical diameter, along which the powers of labor are normally directed). The "two-armed lever" effect is therefore inevitably lost, and the force of traction is distributed equally to the two poles of the head. The result is that the sinciput is brought to the pelvic outlet simultaneously with the occiput. In consequence of this abnormality the sinciput stems against the tip of the sacrum, and the occiput impinges against the ischiopubic rami before it can reach the tuberosities.

The occiput is thus brought into relation with a transverse diameter of the outlet which is much narrower than the bituberal diameter.

THE AVAILABLE TRANSVERSE DIAMETER OF THE OUTLET

Granting that the available transverse diameter is reduced, as a result of deflexion, it is conceivable that there may be an associated compensatory increase in the length of the posterior sagittal diameter.

Measurements were therefore taken in a series of 56 funnel pelves to determine the possible changes in the length of the posterior sagittal diameter, resulting from a displacement of the transverse diameter anteriorly toward the pubis. These determinations were made as follows:

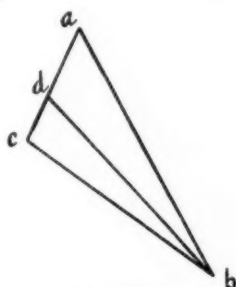


Fig. 1.

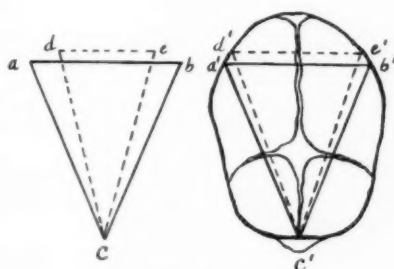


Fig. 2.

Fig. 1.—Sagittal view of pelvic outlet. *ab*, *bc*, and *ac*, represent the sacropubic, the posterior sagittal, and the anterior sagittal diameters, respectively. *bd* represents the posterior sagittal diameter when the transverse diameter is advanced toward the pubis. The gain in length of the posterior sagittal (*bd*), at any particular level depends chiefly on the relative length of the sacropubic and posterior sagittal diameters, *ab* and *bc*, respectively.

Fig. 2.—Cephalopelvic relation at the outlet. *abc* is the triangle of the outlet, formed by the tubera of the ischium (*ab*), and the tip of the sacrum (*c*). *a'b'c'* represents the corresponding triangle of the head. The two triangles are equal; there is no disproportion. *dec* is the triangle of the outlet when the transverse diameter is advanced so far toward the pubis that a reduction of 3 cm. in its width results. *d'e'c'* represents the corresponding triangle of the head. The triangle of the head is much larger than the triangle of the outlet; there is marked disproportion. $\times \frac{1}{4}$.

The bituberal and posterior sagittal diameters were measured in the usual manner by means of a pelvimeter and a series of gauges previously described.⁴ In each instance a gauge, 3 cm. narrower than the bituberal diameter in the particular case, was fitted between the pubic rami, and the posterior sagittal diameter was again measured. It was found that there is an increase of only 0.2 to 1.0 cm. (average 0.48) in the length of the posterior sagittal diameter at the new level; the increase being practically negligible in pelves with a narrow sacropubic diameter (Fig. 1). It is obvious, then, that if the transverse diameter of the outlet is advanced anteriorly toward the pubis, much more is lost in its width than is gained in the length of the corresponding posterior sagittal diameter. The result is that the head is forced to pass through a triangle of the outlet which is much smaller in area than that formed by the tubera of the ischium and tip of the sacrum (Fig. 2).

TRANSVERSE DIAMETER OF THE PRESENTING PART

In consequence of the slight increase in the length of the posterior sagittal diameter coincident with the anterior advancement of the transverse diameter, a segment of the occiput which is considerably reduced in width is brought into relation with the pelvic outlet. It is, therefore, necessary to determine to what extent this diminution in the transverse diameter of the presenting part can compensate for the narrowing of the available transverse diameter of the outlet. This was determined as follows:

The parietal bosses were marked, and the biparietal diameter was measured between these points in the usual manner. Points were then marked on the occiput 2 cm. from the original markings, in a straight line toward the occipital protuberance, and the distance between these points was likewise measured. These measurements were taken in 55 newborns six to nine days old. It was found that on an average the width of the occiput as measured in the manner described, is only 0.72 cm. less than the width of the biparietal diameter. It is clear, therefore, that the gain in length of the posterior sagittal diameter, plus the coincident reduction in the width of the presenting part, compensates for less than one-half of the disproportion resulting from the loss in the width of the available transverse diameter of the outlet (Fig. 2).

THE NARROW SACROPUBIC DIAMETER

The disproportion resulting from deflexion is even greater in funnel pelves with a coexistent contraction in the sacropubic diameter. This is due to the circumstance that the compensatory gain in length of the posterior sagittal diameter is less when the sacropubic diameter is relatively narrow (Fig. 2). In consequence of the shortness of the posterior sagittal diameter the presenting part is advanced anteriorly toward the pubis, and a wider segment of the occiput is brought into relation with the transverse diameter of the outlet. The loss in length of the posterior sagittal diameter, coupled with the increase in width of the presenting part, thus, adds greatly to the disproportion in funnel pelves (Fig. 2).

PRACTICAL BEARING ON TREATMENT

The foregoing analysis of the mechanism of labor shows clearly that pelves with outlet measurements adequate for spontaneous delivery, may be much too contracted for forceps delivery. The minimum values for the dimensions of the outlet used at present as a basis for the management of labor in funnel pelves³ should, therefore, be considerably raised when applied to forceps delivery, particularly in pelves with a narrow sacropubic diameter. The high fetal mortality reported in the recent literature demands a wider margin of safety for forceps delivery than that taken heretofore.

Even under the most favorable circumstances, the forceps should, however, be regarded as a poor substitute for the normal powers of labor. If delivery through the natural passages is decided upon, a policy of ultraconservatism should therefore be followed, and the forceps should be held in reserve to be used only on the strictest indications. Forceps delivery in funnel pelvis should be regarded as a hazardous undertaking, and as a procedure of necessity; not as one of choice or "convenience."

SUMMARY

1. Attention is called to the fact that there is a high fetal mortality incident to forceps delivery in funnel pelvis.

2. A study of the mechanism of labor in funnel pelvis is presented which indicates that the obstruction encountered in forceps delivery is usually due not to preexistent disproportion, but to disproportion resulting from deflexion incident to forceps traction.

3. Deflexion is particularly likely to result in disproportion when there is a coexistent contraction in the sacropubic diameter.

4. The present study substantiates the view long entertained that forceps delivery is usually contraindicated in funnel pelvis.

ADDENDUM

The occipitoposterior position.—In reviewing the case histories since the manuscript was submitted for publication I observed that in 9 out of the 14 cases of attempted forceps delivery in funnel pelvis, labor was complicated by the occipitoposterior position. The malposition was corrected in every one of these cases preliminary to forceps traction; some degree of deflexion characteristic of occipitoposterior positions, however persisted. The disproportion in these 9 cases must, therefore, be attributed in part to the faulty attitude originally associated with the posterior position, which forceps traction failed to correct.

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1009 MEDICO-DENTAL BUILDING

Morrison, Marriott T.: *Chancre of the Cervix*, Am. J. Syph. & Neurol. 18: 196, 1934.

Primary chancre of the cervix, if looked for, is likely to show an incidence of 14 per cent to 18 per cent of all infectious syphilitic lesions in the female. Three-fourths of the cases of primary cervical chancre have gross physical findings that are characteristic. The dark-field examination is the most useful diagnostic procedure.

C. O. MALAND.

SECONDARY PURPURA HEMORRHAGICA COMPLICATING PREGNANCY

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PURPURA hemorrhagica is, according to the literature, a rare but not infrequent complication of pregnancy and the puerperium. The purpuras have been classified by Pratt (*Modern Medicine*, Osler and McCrae, ed. 2, p. 687) into two main groups: the primary and the secondary. The primary, or, as it is better known, idiopathic thrombopenic purpura, is due to a disturbance of the physiologic function of the spleen. In the secondary type, the purpura is a symptom of a known disease or condition, or related to it.

The following two cases were observed in the University Hospital and are presented in the hope that they may answer some of the questions of similar cases.

CASE 1.—Colored female, aged nineteen, admitted Nov. 25, 1931, complaining of lower abdominal cramps. She was one of fifteen children, ten of whom were living and well, the other five having died as children from upper respiratory infections. Her father died at sixty-two from diabetes and her mother at fifty-four from cardiac disease. She had had measles and mumps during childhood. She contracted both syphilis and gonorrhea shortly after her marriage, in 1928, at fifteen years of age. She was delivered at term of her first child, Feb. 17, 1931, after a normal labor. The child was normal. During her pregnancy and up to the time of her present admission she had been under treatment for her two venereal diseases. The patient menstruated May 16, 1931, three months after her delivery, and became pregnant shortly thereafter, the expected date being Feb. 23, 1932. The pregnancy progressed uneventfully. She visited the dispensary on November 5 and at that time was well. On November 25, about 10 A.M. she began to experience lower abdominal cramps simulating labor pains and was admitted to the hospital at 12:30 P.M. On admission the temperature was 98.2° F., pulse 64, and respiration 20. The general physical examination was negative. The uterus was the size of a seven months' pregnancy. No fetal heart could be heard. Believing the patient to be in threatened labor she was given morphine sulphate grains $\frac{1}{4}$ and scopolamine grains $\frac{1}{150}$. At 4 P.M. there occurred a sudden vaginal hemorrhage of about 500 c.c. The uterus was firmer than previously, of the size of an eight months' gestation, and contracting at irregular intervals. The cervix was thin, dilated one finger, but there was no evidence of placenta previa. Shortly after this the patient began to bleed from the mucous membranes of the nose, mouth, and rectum. The urine was clear, acid, specific gravity, 1.016, albumin and sugar negative and microscopically negative. The hemoglobin was 61 per cent (Sahli); R.B.C. 3,500,000; the bleeding time (Duke) was three hours; and an intravenous specimen of blood taken for typing had not formed a clot fourteen hours later. Blood platelet count unfortunately was not done.

At 6 P.M. the pulse was 64, the blood pressure 70/50, and the patient was pale and restless. There was frank hemorrhage from the gums and the patient vomited large quantities of coffee brown material several times. The uterine contractions were every ten minutes and the uterus was stony hard with fundus almost to the ensiform. There was only slight vaginal bleeding. The cervix then was thin and dilated 3 cm. with membranes protruding through the os.

A diagnosis of premature separation of the placenta with retroplacental hemorrhage, complicating or complicated by a purpura, was made. To lessen uterine tension, the membranes were ruptured artificially and a tight binder applied. Labor progressed rapidly and at 8:50 P.M. the patient delivered herself of a stillborn premature female. Following the delivery of the fetus the placenta and many large blood clots were expelled. The placenta showed definite signs of a premature separation.

The uterus contracted well but in spite of pituitrin, ergot, and thromboplastin the bleeding continued. The uterine arteries were ligated by the vaginal route. The uterus and vagina were packed tightly. While this was being done the patient received 1,000 c.c. of normal saline intravenously, followed immediately by 500 c.c. of citrated blood. Continuous hypodermoclysis (2,000 c.c.) was carried out through the night and the patient was given two 15 c.c. doses of thromboplastin. All hemorrhage was well controlled by the next morning, when she was given another transfusion of 450 c.c. of citrated blood. Calcium lactate was given four times daily in 10 gr. doses. The bleeding time was now three minutes and venous blood coagulated in six minutes with a normally firmly retracted clot. The platelet count after the second transfusion was only 158,000.

On November 27 the hemoglobin was 35 per cent and the R.B.C. 2,500,000. There was no further bleeding. A third transfusion of 450 c.c. of citrated blood was given. The vaginouterine pack was removed on November 28. The patient made an uneventful recovery and was dismissed from the hospital December 9, the fourteenth day. The hemoglobin was 53 per cent and the R.B.C. 3,000,000.

The patient was advised to continue her antisyphilitic treatments, calcium by mouth, diet and not to become pregnant. She faithfully performed the first two injunctions but became pregnant during June, 1932, as her last period occurred June 1. The expected date of delivery being estimated as March 8, 1933. During the pregnancy she received the quartz-light weekly, cod liver oil with viosterol 1 c.c., and calcium lactate 10 gr. daily. She also continued her antisyphilitic treatments. The pregnancy proceeded normally until Feb. 5, 1933, when she had a small vaginal hemorrhage of about one hour in duration and just enough to saturate several pads. She was admitted to the hospital. Examination revealed an uterus the size of an eight months' gestation. The fetal heart rate was 140. The placenta souffle was heard in the lower left abdomen just above the symphysis. Vaginal examination failed to reveal any further evidence of placenta previa. The urine was negative. Bleeding time was three minutes, coagulation time three and one-half minutes, platelet count 320,000, and blood serum calcium 10 mg. per 100 c.c.

There was no further bleeding and the patient was dismissed February 8. She was readmitted March 13, 1933, for induction of labor. The bleeding time was three minutes; the coagulation time, nine and one-half minutes; the platelet count, 250,000; the hemoglobin, 61 per cent, and the R.B.C., 4,000,000.

On March 15 she was given 10 c.c. of a 10 per cent calcium gluconate solution intravenously. A medical induction was done March 16 but was unsuccessful. The induction was repeated March 18, and the patient fell into active labor. When the cervix was almost fully dilated she was given another 10 c.c. of 10 per cent calcium gluconate intravenously. She delivered herself spontaneously of a normal male child. The placenta was expressed, and there was only about 150 c.c. of hemorrhage, the blood clotting almost immediately. She was dismissed on the tenth day and has continued to be well without further purpuric symptoms and without treatment.

CASE 2.—White, aged thirty-three, admitted May 8, 1933. The patient had had measles, mumps, smallpox, and scarlet fever. She had had five previous pregnancies, all normal and without any complication. The family history was negative. The last menstrual period began Sept. 25, 1932, following which there was complete

amenorrhea. Quickening was noted in February. There had been occasional headache and vertigo. For three days prior to admission there had been headache, vertigo and some nausea, and she experienced some false labor pains. On the morning of admission while doing some housework she fainted. On regaining consciousness she vomited several times, the vomitus containing coffee brown material. She also noticed a diffuse bilateral conjunctival hemorrhage with a large ecchymosis of the soft tissues surrounding each eye. Nausea, vomiting, and vertigo continued. Labor pains recommenced and she was admitted to the hospital.

On admission a physical examination revealed a fairly well-nourished female who appeared quite ill. There were present the diffuse subconjunctival hemorrhages and ecchymoses of the eyes, each area about 6 cm. in diameter. The fundus of each eye was negative except for slight edema. All the teeth of the upper jaw had been removed, but the lower teeth showed considerable caries. The heart and lungs were negative. The blood pressure was 108/80. The abdomen was enlarged by a seven and one-half months' gestation. The uterus was contracting at irregular intervals. No fetal heart tones or placental souffle could be heard. On rectal examination no dilation or effacement of the cervix could be determined. The extremities were negative except for a large ecchymosis on the dorsum of the right foot.

The urine on a catheterized specimen was of reddish color, 1,020, acid, sugar negative, albumin 2-plus; on microscopic examination there was a rare leucocyte, 30 to 70 R.B.C. per high power field, and many granular casts. The blood Hb. was 65 per cent (Sahli); R.B.C., 3,280,000; W.B.C., 8,000 with a normal differential; platelets 142,000. Coagulation time nine minutes, bleeding time 5.5 minutes. Blood serum calcium 8.9 mg. Nonprotein nitrogen 29 mg. per cent. Wassermann negative. The labor pains disappeared a few hours after admission, the nausea and vertigo ceased. On the following day the patient felt much improved, there was no further vomiting, and the urine appeared macroscopically less red. There appeared, however, a large crop of petechiae over the lower right abdominal wall, and around the neck with a few isolated areas elsewhere.

On May 12 (the fourth day) the petechiae were fading but there was no change in the eyes. The urine had cleared entirely of blood. Fetal movements were absent and no heart tones could be heard. On May 15 there was a slight icteric tint to the skin. On May 19 at 5 A.M. the patient fell into actual labor and delivered spontaneously at 10 A.M. of a dead born macerated fetus. The placenta separated spontaneously and was delivered intact. There was very little bleeding, the uterus contracting well. There were no further purpuric manifestations and the eyes cleared gradually. The patient was dismissed on May 29, and has remained well to date.

DISCUSSION

CASE 1.—The cause of the purpura here is not definitely proved but thought to be on a toxic basis. The possible origins of the toxin are:

1. Arsenic from the antisyphilitic treatment, but there had been no treatment for ten days.
2. Metabolic, as a result of disturbance of metabolism brought about by pregnancy, similar to the toxins causing the various toxemias of pregnancy.
3. Metabolic, as a result of the retroplacental hemorrhage associated with the ablatio placentae. Possibly some change in the blood proteins was brought about with the accumulation of large amounts of blood behind the placenta and undoubtedly infiltrating the uterus. This was reabsorbed by the body tissues and purpura resulted.

An argument in favor of this particular origin is that the onset was so abrupt with no prodromal symptoms.

This case is particularly interesting in another way, and that is the patient's safe conduct through a subsequent pregnancy with many prophylactic measures instituted to prevent the recurrence of the purpura. The majority of patients die as a result of the first attack of purpura during their pregnancy. Repeated pregnancies, therefore, are a little unusual.

CASE 2.—Here as in the first case the etiology is unknown but again presumed to be toxic and probably metabolic on the same basis as the other toxic conditions of pregnancy.

The onset was slow with prodromal symptoms, the course much milder, and the patient received practically no treatment. This is of course in great contrast to the first case.

IMMANUEL DEACONESS INSTITUTE

PREGNANCY AFTER NEPHRECTOMY

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H B. MATTHEWS¹ has collected 241 cases of nephrectomized women with 265 labors, of which 250 were normal and 15 were complicated. Two of his patients died.

He argues very strongly that there was no indication for the immediate termination of pregnancy on discovery of nephrectomy in the patient. He concludes that pregnancy after nephrectomy follows its normal evolution, and that it is little more hazardous for the mother and child than pregnancy under normal conditions, providing the remaining kidney is functioning properly. In cases where nephrectomy has been performed for renal tuberculosis, it is imperative to ascertain whether the patient is free from symptoms of tuberculosis in the bladder, ureter, remaining kidney, and lungs for three or more years before pregnancy is allowed to supervene. Pregnancy after nephrectomy for carcinoma should not be allowed under any circumstances. Pregnancy after nephrectomy should be terminated immediately on the advent of frank renal insufficiency. An albuminuria varying from slight to very marked is to be expected in a certain proportion of cases in the last four or six weeks of pregnancy. This clears up under appropriate treatment.

Kanter and Klawans² in a recent paper on sterilization claim that tuberculosis of the kidney precludes pregnancy even though the focus of infection has been removed by nephrectomy. They hasten to add that they do not mean that every case of nephrectomy calls for sterilization. They have had several cases of women with nephrectomy who were successfully delivered and who made an uneventful recovery. Therefore, they say that previous nephrectomy is not an indication for sterilization unless in cases where the kidney has been removed for tuberculosis or where the function of the remaining kidney is found by laboratory test to be below normal.

Matthews suggests that a more scientific study of the nephrectomized woman be made and that a well "worked-up" report, including all laboratory methods for the determination of kidney function and urinary excretion, should be published of every case of pregnancy after nephrectomy.

Therefore, I am presenting the following case of a pregnant woman with a left nephrectomy for pyonephrosis performed eight years before pregnancy. The case is further complicated by the fact that the woman was extremely obese, aged forty-one years, and a primipara.

E. H. (No. 37523), colored, forty-one years of age, admitted to the Obstetrical Service of Harlem Hospital from the Out-Patient Department on Oct. 27, 1933, at 7 P.M. She complained of dizziness and of having fainted five days previously. The same picture was repeated two days later and upon attending the Out-Patient Department she was asked to come into the hospital.

Patient had had appendectomy performed in 1914. In addition a left nephrectomy for pyonephrosis was performed in Pittsburgh in 1925.

She had an epistaxis twice in August, 1933, and once in September and once (slight) two days before admission. In addition patient claimed palpitation of the heart for a month up to admission. Nausea and faintness and edema of ankles for same period. Her last menstrual period was February 9, 1933, lasting five days. Previous menstruation normal. Para 0, abortions (induced) 4, gravid 5. Pregnant eight months. Examination showed an extremely obese colored woman, weight 218 pounds.

Blood pressure 180/95. Temperature 98.7° F. Pulse 90. Urine: Sp. Gr. 1,018, reaction acid, albumin +++, very many leucocytes. Blood chemistry: creatinin, 1.3 mg. per 100 c.c. blood, urea 8 mg. per 100 c.c. blood, sugar 103 mg. per 100 c.c. blood. Kahn test negative.

Upon a diagnosis of preeclampsias, a Mosenthal test was done and repeated several times. The first Mosenthal test, from urine taken October 29, 12 M. to 8 P.M., showed a specific gravity varying from 1,004 to 1,010.

The pelvis was ample, the presentation vertex, and the fetal position L.O.A.

The patient was kept in bed, bromides and chloral hydrate prescribed, and a low protein content, salt-free diet ordered.

Two hours after admission blood pressure dropped to 160/95. Blood pressure on the day following admission was 136/90, temperature and pulse flat. Urine showed Sp. Gr. 1,012, faint traces of albumin, a few leucocytes. No edema was present.

Three days after admission a urologic consultation was held, and blood pressure remaining normal, urine proving albumin-free, no edema manifesting itself, and a repeated Mosenthal test indicating normal kidney function, it was decided to allow the patient to go to term rather than end the pregnancy.

On the eighth day after admission blood pressure, pulse, temperature, and urine were essentially negative. At this time it was thought that a cesarean section with sterilization might be performed in view of the patient's age (forty-one) and primiparity. The patient was unwilling to give any information about her husband so that his consent might be obtained in writing. It was, therefore, decided to allow the patient to go to term and perhaps deliver spontaneously. A Mosenthal test was taken on the eighth day and revealed a variation in specific gravity of 1,008 to 1,020 in twenty-four hours.

Blood pressure and urine remained normal until the twentieth day after admission. On that day at 12:25 A.M., the membranes ruptured spontaneously. Labor pains did not begin until 1 P.M. The first stage of labor lasted until 7:30 A.M. the next day, or twenty-one hours.

At 10 A.M. the cervix had been fully dilated for more than two hours, and large quantities of meconium were passed. The head was on the perineum, and the patient was having strong pains but making no progress. The blood pressure was 170/110, and the fetal heart was 180. A fibroid 4 cm. in diameter was palpated on the left cornu of the uterus.

In view of these signs of preeclamptic toxemia, fetal distress, age, and primiparity of the patient, a low DeWees forceps delivery was done. A male infant weighing 8 pounds 6¼ ounces was delivered. A tight loop of cord around the neck was freed and resuscitation successfully applied.

There was a first-degree laceration of the perineum. The placenta was expressed thirty minutes after delivery and 1 c.c. of pituitrin and gynergen was administered.

The day following delivery the blood pressure was 144/88, urine findings were negative, and the general condition was good.

Three days after delivery the patient complained of pain in the left chest, but examination was negative. Two days later blood pressure, temperature, pulse, and urine were normal. There was a profuse lochia, slightly foul, the abdomen was slightly distended, and the fundus was two fingers below the umbilicus.

On the sixth day postpartum the patient complained of drowsiness and night sweats but no cough. Blood pressure, pulse, and temperature were normal, and the urine showed a specific gravity of 1,018, albumin ++, and a moderate number of leucocytes.

The next day the patient complained again of profuse night sweats, but the general condition was good. Breasts were moderately engorged and tender. Abdomen was relaxed, the fundus was well involuted and firm. Lochia was profuse and foul. Blood pressure, pulse, and temperature were normal. Urine showed specific gravity 1,018, albumin +, and a few epithelial cells.

On the tenth day, the thirty-first day after admission, the patient left the hospital.

The patient returned to the follow-up clinic four weeks later having worked as housekeeper for the past two weeks. Blood pressure 150/90. Vaginal examination: perineum healed and firm, introitus roomy, cervix smooth and closed, uterus anterior, freely movable, well involuted, small fibroid felt on fundus, adnexa negative. Urine: color straw, clear, Sp. Gr. 1,024, trace of albumin, glucose negative, few epithelial cells.

April 16, 1934: Patient had continued working. Examination negative. Urine: color straw, Sp. Gr. 1,016, albumin +, glucose negative. Microscopic examination of urine: few epithelial cells, occasional white blood cells, acetone negative, diacetic acid negative. Blood chemistry: creatinine 1.3 mg. per 100 c.c. blood, urea nitrogen 9.6 mg. per 100 c.c. blood, sugar 96.0 mg. per 100 c.c. blood. Blood pressure 130/90.

CONCLUSIONS

Despite nephrectomy, advanced age, obesity, and primiparity of the patient, she was successfully delivered of a living child with the use of low forceps.

Albuminuria, high blood pressure, vertigo, and edema were cleared up prior to delivery by use of low protein content, salt-free diet, and rest.

The patient was carefully watched by means of constant blood pressure readings, urinalyses, and repeated Mosenthal tests for insufficient kidney function. The determination was to terminate pregnancy immediately if these manifested themselves.

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1132 PARK AVENUE

SUDDEN DEATH DUE TO PULMONARY EMBOLISM IN A CASE
OF PUERPERAL ENDOMETRITIS ASSOCIATED WITH
UNSUSPECTED SUPPURATION IN THE
RUPTURED SYMPHYSIS PUBIS*

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SEPARATION of the symphysis during labor or delivery is not uncommon, but suppuration into the ruptured symphyseal joint is of rare occurrence, and it is the accidental finding of this condition at autopsy that warrants this case report.

F. B., a white American housewife twenty-four years old, was admitted Feb. 7, 1934, with a history of ruptured membranes for four hours and mild pains for six hours. The patient had been attending the prenatal clinic and the pregnancy had been normal throughout the antepartum course. The family history and past medical history were completely negative except that she had undergone two operations previously; a thyroidectomy two years before and the removal of an ovarian cyst and appendix one year before. The menstrual history was normal, the last normal period May 2, 1933, the expected date of confinement Feb. 9, 1934. She had had two full-term living children. The first of these was a spontaneous delivery after a three-day labor; the second was a low forceps delivery after an eighteen-hour labor. No suturing was required after either delivery and the postpartum course was perfectly normal each time.

Physical examination at time of admission showed a well-developed woman. Temperature, pulse, and respirations were normal. Blood pressure was 110/70. Abdominal examination revealed an old scar in the lower midline and a full-term uterus with the fetus in the L.O.A. position. The fetal heart sounds were in the L.L.Q., 140 and regular. The vertex was floating. The external measurements were: interspinous 21, intercrystal 26, right oblique 21 cm., left oblique 21 cm., and external conjugate 17.5 cm. Vaginal examination revealed a moderate cystocele, the cervix was thick, uneffaced, one finger dilated, and the promontory was easily reached. The outlet seemed to be ample. The diagonal conjugate measured 11.5 cm., giving a true conjugate of about 10 cm. The baby was not big, and as the head could be very easily pressed into the brim, the impression was that delivery would easily occur from below, once real labor set in.

For the next thirty-eight hours the patient continued to have moderately severe uterine contractions at five- or six-minute intervals. These had no effect on the cervix, which remained thick, uneffaced, and one-finger dilated; and the vertex remained high and unengaged. During this period she was given two doses of $\frac{1}{6}$ gr. of morphine and $\frac{1}{150}$ gr. of scopolamine, each of which gave her about three hours of rest. After the second injection had worn off, a hot soapsuds enema and 2 ounces of castor oil were given, with the hope of initiating effectual uterine contractions, but without success. Temperature, pulse, and respirations were still normal, blood pressure 110/70, urine negative, and the patient was taking food and fluids well.

Forty-four hours after the onset of pains, the patient was taken to the delivery room and a No. 5 Voorhees bag was easily inserted into the cervix without any anesthesia. The patient was then put back to bed and a one-pound weight was at-

*Presented at a meeting of the Brooklyn Gynecological Society, May 4, 1934.

tached from the bag over the lower pole of the bed. This was followed by fairly strong contractions in about one and a half hours and the bag was expelled eight hours after its insertion. A full-term normal baby in the L.O.A. position was born spontaneously two hours after the expulsion of the bag. No anesthesia was used. There were no soft tissue tears at the time of delivery. The placenta and membranes were delivered spontaneously and apparently completely, ten minutes after the birth of the baby. The total blood loss was about 200 c.c. Both pituitrin and gynergen were given hypodermically after the expulsion of the placenta as the uterus showed a tendency to relax. This was supplemented with fluid extract of ergot.

The duration of the first stage was fifty-four hours, the second stage a little less than an hour, and the third stage ten minutes. The number of vaginal examinations was 3, rectal examinations 10. At time of delivery the temperature was 101.4°, pulse 100, respirations 20.

Second Day Postpartum: Temperature 102.6°, pulse 120, respirations 24. Patient complaining of pain in lower abdomen over the symphysis and across the lower back. Could not lift legs or turn on side without excruciating pain in the symphysis, back, and along both thighs and legs. Physical examination revealed a definite separation of the symphysis with marked tenderness over the symphysis pubis and over both sacroiliac regions. An x-ray taken on this day showed "slight diastasis of the symphysis pubis and slight downward displacement of the left pubis." The pelvis was tightly strapped with adhesive in the form of a many-tailed binder with marked relief of symptoms. This strapping made it possible for the patient to turn and to move her legs after it had been on for twenty-four hours. After this, the pain and tenderness gradually disappeared, and the strapping was removed eight days after its application. At the time of its removal, the symphysis still felt separated, but all symptoms were gone.

The patient ran three complete cycles of temperature of three days each, the temperature fluctuating from 101° to 103.5°. The lochia remained scant and foul, the uterus subinvolved, and there was moderate tenderness over both parametrial areas and also over the symphysis. The treatment during these ten days consisted of immobilization of the pelvis, high Fowler's position, ergot, fluids, ice bag, codeine and aspirin for pain, and sodium amytal for rest at night. There were no chills at any time.

On the tenth day postpartum, the temperature came down to normal and after fluctuating from 98° to 100° for two days, it remained normal after the twelfth postpartum day. On the fourteenth day the patient was allowed out of bed for a short time. After being up for about fifteen minutes, she walked to the bathroom, which was only some ten feet away, and shortly called the nurse, stating that she felt very faint. The nurse put the patient's head between her knees and in doing so, noticed that the patient was unconscious. She was carried back to her bed by nurses and internes. Patient was in coma, and pulse very rapid, thready, and feeble. She was very pale and cyanosis developed rapidly about the nose and mouth. Adrenalin, intramuscularly and intracardiac, were given. Oxygen and artificial respiration met with no response. Patient was pronounced dead twenty-five minutes after complaint of feeling faint.

The autopsy showed neither the peritoneal nor the pleural cavities with free fluid or adhesions.

The lungs were reddish blue in color; there was marked congestion and edema at the bases; the left lower lobe showed a few small reddish patches of consolidation which appeared to be an early bronchopneumonia. In the lower half of the left lower lobe there was an area about two inches in diameter which was dark red, firm, and sharply demarcated from the rest of the lung. On opening the branch of the pulmonary artery running into the left lower lobe, there was found to be a large

embolus, well organized, grayish red in color, and adherent to the vessel wall. The pericardial sac contained about 20 c.c. of fluid blood, and there was a needle puncture on the anterior surface of the right ventricle. The heart was normal in size; the myocardium was pale red and firm on section. The cardiac valves showed no gross pathology. The aorta was grossly normal. The spleen was enlarged, weighing 220 gm. Its surface was slate blue. On section, the pulp was dark red, soft, and pulpaceous. The liver was of normal size; surface was smooth, but was rather soft in consistency. On section, the parenchyma was of a mahogany red color, with areas of yellowish mottling scattered throughout. The kidneys were normal in size; capsules stripped easily, leaving smooth surfaces. On section, the cut surfaces were light red in color; cortices were normal in size, markings stood out prominently. Gastrointestinal tract showed no gross pathology.

Uterus was enlarged to about the size of a three and a half months' pregnancy, the fundus extended about two inches above the pelvic brim and was soft in consistency. The cervix showed no lacerations or erosions. On opening the uterus, there was found an area 2 x 2 inches on the upper posterior wall which was covered with reddish black, soft, friable tissue which was adherent to the uterine wall. Sections through this area showed a purulent exudate in the walls of the uterus.

The veins of the right broad ligament were enlarged, thickened, and filled with blood clot. The right ovarian vein was thickened to about the size of one's thumb finger and was filled with an organized thrombus. The iliac veins appeared normal. Tubes and ovaries appeared grossly normal. On section, the ovaries were found to be fibrocystic.

There was a marked separation of the symphysis pubis in the midline and upon incising the symphyseal joint, about one dram of thick, yellowish, odorless, purulent exudate escaped. There was no evidence of any infection in the space of Retzius nor was there any gross evidence of any osteomyelitis of either pubic bone.

Anatomic Diagnosis.—Congestion and edema of lungs; bronchopneumonia; pulmonary embolism; hemorrhagic infarction of lungs; cloudy swelling of heart, liver, and kidneys; congestion of spleen; septic metritis and endometritis; thrombosis of veins of right broad ligament and right ovarian vein; chronic fibrocystic oophoritis; and separation of symphysis pubis with suppuration.

Cause of Death.—Pulmonary embolism following septic endometritis and metritis.

1325 UNION STREET

Hirsch-Hoffman: The Development of Tuberculosis of the Female Genitalia and Peritoneum in Primary Infections of the Intestinal Tract, Arch. f. Gynäk. 153: 375, 1933.

The author does not believe that primary tuberculosis of the female genitalia exists, but that all genital infections are secondary. Such secondary infection may result from contact, from extension of peritoneal infection to tubal lumen or by way of the lymphatics or the blood stream. The comparative frequency of these four methods of infection is unknown. The author reports the results of his experimental work on rabbits and his studies on some of the nurslings who died during the ill-fated tuberculosis inoculations in Luebeck.

He concludes that in severe primary intestinal tuberculosis the peritoneal infection is primarily lymphogenic. In infection of the female genitalia the infection may be lymphogenic or hematogenous in origin. The transtubal development of tuberculous infections of the female genitalia is much less frequent than are the lymphogenic or hematogenous infections.

RALPH A. REIS.

BILATERAL URETEROVAGINAL FISTULA

SUCCESSFUL IMPLANTATION OF BOTH URETERS INTO THE BLADDER SEVEN AND ELEVEN MONTHS FOLLOWING TOTAL HYSTERECTOMY

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IN ALMOST all the cases of severance of the ureter, recognized during operation, there is a possibility of repairing the damage by ureteroureteral anastomosis ligature, or implantation of the ureter into the bladder. In a small number of these cases and in cases of partial damage to the wall of the ureter, however, a ureterovaginal fistula may develop, which is the unavoidable outcome if the injury of the ureter has not been recognized during operation. There is a chance that a ureterovaginal fistula may heal spontaneously either with full function of the kidney or by autonephrectomy as much as three months following operation. After this time a secondary implantation has to be attempted. According to Bland, secondary implantation, owing to envelopment of the damaged end of the ureter in fibrous tissue, is extremely difficult and infinitely more so than primary implantation. Kermauner, considering the difficulties of secondary implantation, advises nephrectomy whenever a ureterovaginal fistula fails to heal spontaneously in three months.

The difficulty and frequent failure of secondary implantation prompts the report of a case with bilateral ureterovaginal fistula cured by implantation of both ureters into the bladder.

Alice B., aged forty-two years, was admitted Sept. 1, 1933. (Hospital No. H 9638.) The patient's one pregnancy had ended in spontaneous miscarriage. During February, 1933, she noticed a bloody vaginal discharge between otherwise normal menstruations. Diagnostic curettage performed February 5 revealed cancer of the cervix. Following local treatment with radium, abdominal radical extirpation of the uterus was performed April 10, 1933. After the operation the patient noticed considerable drainage of urine through the vagina, although she was able to void. Except for this condition she felt well and had gained in weight just prior to her entrance into the hospital, her weight being 104½ pounds.

Examination on admission to the University Hospital revealed a fair general condition and no organic disease. The vagina was long, soft, and without infiltration of vaginal stump or paravaginal tissue. Rectal exploration gave no evidence of a local return. After exposing the vaginal fornix, urine could be seen draining through the fistula into the vagina. The bladder was filled with a solution of indigocarmine, but no colored fluid drained into the vagina, nor was the amount of drainage increased. The diagnosis of ureterovaginal fistula was made. After having given the patient a good rest and daily sitz baths for ten days, cystoscopy was performed on September 11 which revealed the following findings: capacity of bladder and mucosa normal. The left ureter showed rhythmical contractions expelling clear urine, and was catheterized without difficulty. The right ureteral ostium was contracted and a catheter could be inserted for only 3 to 5 mm. Four minutes following the intravenous injection of indigocarmine, clouds of blue urine were passed through the left ostium, while on the right a scarcely perceptible amount of stained urine appeared only at long intervals. After another attempt to introduce a catheter into the

right ureter, the secretion on this side stopped entirely. The exposure of the vaginal fornix now showed definitely the opening of the fistula, through which the stained urine was spurting at rhythmical intervals. A catheter could easily be inserted through the fistula into the ureter and pushed up into the pelvis of the right kidney. The intravenous pyelogram showed a perfectly normal condition of both kidneys. From these findings it was concluded that there was a fistula of the right ureter, located near its insertion into the bladder, and, therefore, its implantation was considered. With the consent of the patient, laparotomy was performed under spinal anesthesia the following day.

Operation September 12, 1933: After having inserted a catheter into the right ureter from the vagina, a median incision was made through the old scar, and many adhesions of the bowels to the peritoneum separated. During the dissection of a loop of bowel, which was extensively attached to the vaginal stump by dense scar tissue, the vagina was opened and the catheter exposed. The peritoneum was split and the ureter dissected and found to be enlarged to the size of a little finger. The enlargement was not caused by dilatation, but by a firm edema of the wall of the ureter. After sufficient mobilization the ureter was split for a few millimeters and each flap caught with a suture. A clamp was introduced into the bladder through the urethra in order to locate the most suitable place for implantation, the wall incised on the tip of the instrument, the end of the two "traction" sutures caught by the forceps, and the ureter pulled into the bladder. The margins of the opening of the bladder were pulled up and fastened wall to wall to the ureter by fine sutures. The peritoneal incision was closed by interrupted sutures, whereby the wall of the bladder was lifted up in order to eliminate as far as possible any tension, and the abdomen closed in layers. Finally the "traction" sutures, which had not been knotted, were pulled out and a retention catheter was inserted into the bladder.

The postoperative course was uneventful. The patient was up on the ninth day and the retention catheter removed on the tenth postoperative day. Sixteen days following the operation the patient was discharged. Examination did not reveal any drainage of urine into the vagina, although a moderate secretion from the granulating vaginal fornix had a urine-like odor. On October 19, twenty days following discharge, the patient was readmitted, complaining that she had been losing urine through the vagina since the second day after her return home, although considerably less than before the operation.

Inspection of the vaginal fornix revealed a granulating sinus exuding some moisture with urinary odor, but no dribbling or spurting of urine. Cystoscopy showed that at the place of implantation one flap of the ureter had retracted and slipped out of the bladder, and only one was protruding into the bladder. The part of the wall of the bladder to which this flap was tightly fixed was retracting and bulging vigorously at rhythmical intervals.

On the pyelogram a definite though moderate hydronephrosis of the formerly normal right kidney was noted. As the ureter was evidently in close connection with the wall of the bladder, another attempt at implantation seemed justified. Laparotomy was performed under spinal anesthesia on November 6 along the old incision, whereby the scarred tissue was excised. After separation of many adhesions the ureter was dissected and found to be slightly dilated, but without any edema of its wall, and fixed to the wall of the bladder. The ureter was severed and split, but this time both flaps were fixed to the wall of the bladder by sutures, according to Sampson, in order to prevent another slipping of the ureter. A retention catheter was inserted into the bladder, and the abdomen closed in the ordinary way. The postoperative course was uneventful, but in order to be sure of the result, the patient was kept in the hospital for twenty days. Six weeks following her discharge the patient returned with a letter from her physician, stating that she had been losing

urine since shortly after discharge in the same amount as before the first operation. She and her husband were determined to have the kidney removed.

The general condition of the patient when she was readmitted on Jan. 8, 1934, had considerably improved, and she had gained fifteen pounds in weight. Inspection of the vaginal fornix gave evidence that the fistula had shrunk, but not entirely closed. No drainage of urine could be seen, but a small amount seemed to have oozed into the vagina during examination. Bilateral pyelograms disclosed that the pelves of the right kidney which had been found dilated prior to the second operation, had become normal.

Studies with the injection of indigocarmine gave evidence of normal function of both ureters and kidneys. The introduction of a catheter into the right ureter failed to keep the patient dry, while the drainage was stopped entirely by catheterizing the left ureter.

Thus it became clear that from the beginning there had been a bilateral ureterovaginal fistula draining through one opening in the right fornix of the vagina. Further studies showed that in order to keep the patient dry it was sufficient to insert the catheter only 2 to 3 cm. into the left ureter. Another pyelogram confirmed the conclusion that the opening in the ureter was near its vesical insertion, so that its implantation into the bladder could be considered. As almost all the urine from the left kidney was found to be emptying into the bladder during this and the previous cystoscopic examinations, no injury of the left ureter had ever been suspected, and it seemed likely that the fistula was a very small one. Knowing that such fine "hair-fistulas" occasionally close spontaneously if kept entirely out of function over a period of time, a catheter was inserted into the left ureter and kept in place for two weeks. Although the patient felt well during this time and was dry, she began to lose urine as soon as the catheter was removed. A third operation was therefore performed on Feb. 6, 1934, under spinal anesthesia after a catheter had been passed into the left ureter. After having separated many adhesions, the peritoneum was split and the left ureter was dissected. The ureter was found moderately dilated and considerably thickened by hard edema, and near its vesical end it was embedded in scar tissue. The ureter was severed near the bladder, split, and pulled into the bladder, where both flaps were fixed to the wall of the bladder by fine catgut sutures. The margins of the bladder incision were pulled upward and fixed to the periureteral tissue by several sutures. After insertion of a retention catheter into the bladder, the abdomen was closed in layers. The postoperative course was uneventful. The retention catheter was removed on the eleventh, and the patient allowed up on the fifteenth day. She was discharged on the seventeenth postoperative day without any leakage of urine.

Since discharge the patient has been treated several times for mild cystitis, but has remained dry. A thorough cystoscopic examination and pyelogram taken five months later showed normal function of both kidneys and ureters.

Although the patient was in perfect health, two possible complications had to be kept in mind, a return of the cancer and the development of a stricture of the right ureter. The ureter, being markedly shortened by the primary injury and the two implantations, was under a permanent axial tension effecting a reduction of its lumen. Under these circumstances even a moderate shrinking of scar tissue was likely to result in a stricture. This actually happened thirteen months following the implantation, when the patient developed an acute attack of hydronephrosis on the right side, which was relieved by introducing a fine catheter into the right ureter. Various attempts to dilate the stricture were unsuccessful, and the right kidney had to be removed.

THE INCIDENCE OF PUERPERAL INFECTION IN PATIENTS DELIVERED IN THE HOSPITAL AS COMPARED TO PATIENTS DELIVERED AT HOME

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FOR many years there has been considerable discussion concerning the incidence of puerperal infection following delivery in the home as contrasted with the lying-in hospital. There have been frequent statements made in the literature to the effect that the average obstetric patient is safer at home than in the hospital, and the following study has been undertaken in an effort to compare the incidence of puerperal infection in institutional and domiciliary practice.

At the outset it was felt that there were two factors which had to be considered in order to present comparable figures: first, the large number of late admissions of abnormal and neglected patients to a hospital service with its resulting high incidence of operative deliveries and its attendant increase in morbidity; and second, the relative lack of postpartum supervision of patients delivered in the home as compared to those in the hospital.

In consideration of the first factor we have included as a control group the cases of multiparas who were delivered spontaneously of viable children without operative induction by bag or bougie on the Hospital Service of the Johns Hopkins Hospital between May 1, 1932, and April 30, 1934, inclusive, and have compared them to multiparas delivered in like manner by the Outside Service during the same period of time. Concerning the second factor, it has long been noted that mild cases of puerperal infection are demonstrable by fever only in the afternoon and evening, and it has been thought that many of them have been missed on the Outside Service owing to the fact that the nurse in making her postpartum visits was able to record only one temperature reading per day, and this usually between the hours of eight and eleven in the morning. Therefore, in order to obtain closer supervision of the cases delivered at home during the years 1933 and 1934, temperatures have been taken every four hours from eight in the morning to eight at night in the following manner: Four thermometers were left at each house in separate envelopes marked with the appropriate hour. The patient was instructed to place each in her mouth for five minutes at the proper time and then to replace each in its envelope for the nurse to read on her morning rounds. Patients were cautioned not to drink hot liquids before taking the temperature and to keep the thermometers

in a cool place when not in use. If fever was noted by the nurse, the externe was immediately notified and the cause investigated.

The criterion employed for a febrile puerperium is that of the Obstetrical Service of the Johns Hopkins Hospital, namely, two elevations of temperature to 100.4° F. or higher on two or more days of the puerperium not necessarily consecutive, and excluding the first twenty-four hours after delivery. A diagnosis of puerperal infection has only been made in those cases in which the fever could not be adequately explained on a basis of pyelitis, upper respiratory infection, mastitis, or other causes, and in whom there was some direct evidence of uterine involvement as shown by abdominal pain and tenderness, foul lochia, and other signs. No patients were included who had been attended during pregnancy or labor by midwives or outside physicians.

Finally, we wish to state that the patients in the series, both hospital and home, comprise material from the tenement district of a large city and are about equally divided between whites and blacks. We, therefore, feel that while this series of cases may not be comparable to another from a different city or class of individuals, they are certainly comparable to each other.

TABLE I. HOSPITAL CASES

May 1, 1932—April 30, 1933

Multiparas delivered spontaneously	340
Cases of puerperal infection	15
Incidence of puerperal infection	4.4%
Febrile, other causes	10

May 1, 1933—April 30, 1934

Multiparas delivered spontaneously	365
Cases of puerperal infection	18
Incidence of puerperal infection	4.9%
Febrile, other causes	10

Table I shows the incidence of cases of puerperal infection among 705 normal women delivered at the Johns Hopkins Hospital during a period of two consecutive years, and it should be pointed out that there is only a very slight difference (0.5 per cent) between one year and the other.

TABLE II. OUTSIDE CASES

May 1, 1932—April 30, 1933

Multiparas delivered spontaneously	479
Cases of puerperal infection	4
Incidence of puerperal infection	0.8%
Febrile, other causes	5

May 1, 1933—April 30, 1934

Multiparas delivered spontaneously	510
Cases of puerperal infection	43
Incidence of puerperal infection	8.4%
Febrile, other causes	5

Table II shows the incidence of puerperal infection as recorded on the Outside Service during the same two-year period and includes 989 cases.

During the years 1932 and 1933, there was but one temperature reading per day taken by the nurse on her morning rounds, while during 1933 and 1934, temperatures every four hours were obtained as described above. The increase in the incidence of puerperal infection from 0.8 per cent to 8.4 per cent is entirely the result of the closer supervision of cases during the second year, since only the nurses' record of morning temperatures had been used, there would have been four rather than forty-three cases diagnosed, a figure identical with that of 1932 and 1933.

That the general character of puerperal infection did not change in the locality in question from one year to the next is suggested by the fact that during each year there were three cases on the Outside Service considered sufficiently severe to warrant transfer to the Hospital, and also by the fact that the average duration of fever for both years as well as its maximum height among the Hospital cases was approximately the same. A careful study of the comparative severity of the infections occurring in the hospital and the home revealed nothing of significance. The height of the temperatures and their duration was about the same in both series of cases. Of the cases included in this study, there was one death on the Hospital Service which followed a prolonged labor of forty-five hours and severe perineal lacerations with an ensuing streptococcus septicemia, and one death on the Outside Service which was the direct result of a fulminating eclampsia. From the similarity of the character of the infections occurring in the two series and from the definitely increased frequency of puerperal infection among patients delivered in the home (8.4 per cent as against 4.69 per cent), we believe that hospitalization of the lying-in woman is an important factor toward her well-being.

CONCLUSIONS

1. The incidence of puerperal infection was almost twice as great in a series of normal women delivered in the home as in a comparative group delivered in the hospital.
2. No difference in the severity of the infection could be elicited between the two groups.
3. This study would seem to indicate that in the modern maternity hospital the patient has a better chance of escaping infection than in the home.

INTESTINAL OBSTRUCTION COMPLICATING PREGNANCY

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THE literature of recent years reveals a comparatively small number of references to intestinal obstruction in pregnancy. The majority of cases reported apparently terminated in premature labor with loss of the child. In many of the cases the mothers were also sacrificed.

DeLee mentions it as a rare complication which may be due to the same causes capable of producing it outside of pregnancy. Curtis in a recent work devotes a small paragraph to the condition and concurs in DeLee's opinion. The greater number of cases reported appear to be the result of abnormal adhesions of the intestines to the uterus, the latter organ in its growth dragging on the intestines and producing complete obstruction. All of the authors are of the opinion that recognition of intestinal obstruction constitutes an imperative indication for surgery and without needless delay. In the majority of cases this is to be followed by induction of labor or such other operative measures as the situation demands.

The case reported herewith appears to be of unusual interest because of the many incidental factors and also because of the fact that after surgical interference for the relief of the obstruction, the pregnancy was successfully carried on and the mother normally delivered at term.

Mrs. B. H., aged twenty-two years, white, nullipara, was first seen on June 10, 1932. She had been married four months. Her previous history was irrelevant. She had had no serious illnesses and no operations. Her menstruation had begun at twelve years of age and had always been of a twenty-eight-day type. No dysmenorrhea.

On the fifteenth of April she menstruated normally. Two weeks following this she passed a small amount of blood, the flow lasting two days. Several days later she had a slight cramplike pain in the lower abdomen which disappeared in a short while. There was no nausea; no unusual soreness of the breasts. She did not menstruate in May. On June 6 after flowing slightly for four or five days she suddenly had sharp pains in the right lower abdomen. This lasted for several hours, then disappeared. She did not faint. On June 10 she had another attack of pain, not as severe, however, as the preceding one and she felt rather faint. I was called to see her for the first time on this date.

Examination revealed a well-developed and nourished female who was rather pale. The general examination was essentially negative. Blood pressure was 110/80, pulse 100, and temperature 98.4°. The abdomen was markedly rigid and tender to pressure over the entire right lower quadrant. Pelvic examination revealed a normal nulliparous introitus. The cervix was soft, a moderate amount of bright red blood presenting. The uterus was slightly enlarged, anteflexed, soft and partly fixed. There was a mass about the size of a lemon in the right tuboovarian region; this was extremely tender. There was an impression of bogginess in the culdesac. Diagnosis of ruptured ectopic pregnancy was made and the patient was admitted to St. John's Hospital.

Operation under spinal anesthesia of 150 mg. of novocaine. A midline incision was made. The peritoneal cavity contained free blood. The right tube, markedly distended, was the seat of laceration at the isthmus. The placenta and embryo had been expelled from the tube and were lying on the anterior surface of the round ligament, and it appeared that the placenta had begun to attach itself at this

point. Placenta and ovum were carefully removed. The broad ligament was clamped and the right tube including its interstitial portion was removed. A simple cyst on the right ovary was punctured. The left tube and ovary were normal. The patient being in good condition, the appendix was removed in the usual manner and the abdomen closed without drainage. Convalescence was uneventful. Examination two months after operation revealed the pelvis in apparently good condition.

Subsequent History.—In May, 1933, the patient presented herself at the office, stating that she was anxious to become pregnant. She had used no contraceptives for three months. Examination revealed the pelvis apparently normal. Carbon dioxide tubal insufflation by the Rubin method was performed. After two attempts using a maximum pressure of 200 mg. the gas entered at 140 mg. and more rapidly at a lower level. She had the typical shoulder pain. The June period was normal. On July 3 she menstruated slightly for two days. A few days later she had a slight pain in the left side. At this time there was some soreness of the breasts. Examination eliciting no pathology she was advised to keep in touch with the office, reporting again in a few days. On July 16 she returned, the slight intermittent bleeding persisting at this time, and she had had slight cramping pains at times in the left side. The uterus appeared slightly enlarged and there was definite thickening about the left uterine cornu; this was quite tender. It appeared that I might be dealing with another ectopic or possibly cornual pregnancy. She was kept under observation. A few days later, following a severe attack of cramps she passed a large clot which, however, was not saved for examination and her symptoms immediately subsided. This would suggest that she might have had an early abortion.

On Jan. 4, 1934, she presented herself at the office complaining of some nausea and soreness of the breasts. Her last menstruation was Nov. 7, 1933. Examination revealed the uterus size of six weeks' pregnancy. The adnexa were apparently normal. The pelvic measurements taken at this time were found to be within normal limits. Term was estimated at about Aug. 14, 1934.

In March she complained of slight increase in nausea and of some cramplike pains in the lower abdomen. The bowels were acting normally and the examination was essentially negative. On April 29 she had what she believed was indigestion. She had a severe pain in the left lower abdomen and was nauseated. Taking on her own initiative, doses of soda followed by enemas, she had several good bowel movements, but continued to have cramplike pains.

Examination at this time revealed rather marked uterine contractions, and it was feared that she might miscarry. No vaginal examination was made. There was no bleeding. She was put at rest and the symptoms subsided after two doses of morphine. For several days she felt very well. On May 1 she vomited several times, was markedly distended; stated that her bowels had not moved for two days. Enemas and the other methods employed being ineffectual, it was decided that complete intestinal obstruction was present and operation was decided on. She was removed to St. John's Hospital.

At operation under spinal anesthesia a left rectus incision at about the level of the umbilicus was made. This point was selected because of the location of the pain and the probability that nothing would be done but an ileostomy. This subsequently proved to be an error. On opening the peritoneal cavity free fluid presented. The patient appearing to be in good condition and no obstruction being noted on the left side, the hand was introduced further and the terminal ileum was found densely adherent to the uterus at the point originally occupied by the right tube. In its growth the uterus had pulled on the intestines, producing an acute angulation. The adhesions were freed and two small injuries to the intestinal serosa were repaired. As the intestines appeared to empty themselves spontaneously one ampule of amphetin was introduced into the peritoneal cavity and the abdomen was closed

without drainage. Gastric lavage was performed on the table, and it was noted that the patient also passed a large amount of gas and liquid stool.

Preoperative and postoperative treatment consisted of frequent intravenous injections of hypertonic saline solution to combat the loss of chlorides; solutions of glucose being given simultaneously. The patient did well until the third postoperative day when there occurred an acute gastric dilatation, and she appeared acutely ill. Gastric lavage through a nasal tube, which was allowed to remain in situ for forty-eight hours, was performed. There was no recurrence of symptoms. On May 8 the bowels moved spontaneously several times and her condition thereafter was quite satisfactory. During this period the child was quite active and no abnormal uterine contractions were noted. She left the hospital in good condition on the twelfth postoperative day. The abdominal wound was well healed.

On June 1 examination revealed the child in the vertex, growing normally. On July 5 she had rather severe Braxton-Hicks contractions which, however, subsided after a small dose of opiate. On July 18 contractions again started and as labor appeared imminent she was admitted to the hospital. The child was in vertex R.O.A. Cervix was rather thick, and dilatation one finger. That evening progress being rather slow, contractions poor and irregular, the cervix dilated three fingers, the membranes were ruptured instrumentally. Contractions were further stimulated with three minum doses of pituitrin given at half-hour intervals. When dilatation had reached $3\frac{1}{2}$ fingers, nitrous oxide anesthesia was administered, progress from then on being fairly rapid. After the head had been expelled from the cervix, forceps were applied after a deep lateral episiotomy and a female child weighing 5 pounds 4 ounces was delivered in R.O.A. Child was in good condition. Placenta and membranes were expelled intact. Episiotomy was repaired. There was no abnormal bleeding. As the mother appeared to be slightly dehydrated, 500 c.c. of 5 per cent glucose was given intravenously. Puerperium was uneventful and the patient left the hospital on the tenth day.

Final examination at the end of six weeks revealed the abdominal wounds well healed. The cervix was normal and the perineum was well healed. The uterus was in good position. The breasts were in good condition, no attempt having been made to nurse the baby.

This case appears to be worthy of comment because of the many factors that were brought into play during the time this patient was under my care. Of interest is the fact that pregnancy followed tubal insufflation; this therapeutic and diagnostic procedure having undoubtedly freed some fine adhesions probably resultant of the original operation.

Spinal anesthesia favored the contraction of the intestines after the adhesions were freed. This apparently forestalled the necessity of intestinal drainage by ileostomy. Amphetin was used following freeing of adhesions in an attempt based on recent clinical reports to prevent their recurrence.

The duodenal tube proved a life-saving measure in the treatment of and prevention of recurrence of gastric dilatation.

With full knowledge of the part played by the unknown factor "luck" in the management of this case it was, however, impressed on me more than ever that the so-called obstetric specialist should be more than a mere midwife, but be trained in and competent to perform such abdominal surgery as can occur as a complicating factor during the course of any pregnancy.

MODIFICATIONS OF THE ASCHHEIM-ZONDEK REACTIONS WITH ABORTION

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DEVIATIONS from the standard changes noted in the ovaries of rats used in the Aschheim-Zondek test, namely, modifications in the intensity or even the absence grossly of one or more of the results termed Reactions I, II, and III, accompanied by an estrous hypertrophy of the uterus may occur so regularly with certain complications of pregnancy that they become important criteria in diagnosis.

When the report by Jeffcoat¹ in 1932 appeared describing these modifications of the Aschheim-Zondek reactions with abortion, independently, the same variations had come to my notice and had been correlated with abortion or impending abortion. Jeffcoat's original description, therefore, is confirmed by my observations.

For each test three immature female white rats, litter mates, twenty-five to thirty days old, were used. Two cubic centimeters of cleanly collected urine was injected intraperitoneally into two rats, twice daily for two days, the third and largest rat being used for a control. Forty-eight to seventy-two hours after the last injection all of the rats were killed and the genitalia examined. In a positive test the results were clear and all three reactions were present grossly in the ovary. When in doubt, the ovaries were removed, one was pressed between glass slides and examined with direct daylight or under the microscope for Reactions I and III. The other ovary after washing was cleared in glycerin overnight in order to bring out Reaction II. The enlargement of the uterus was always apparent grossly.

The urine of women aborting or with impending abortion caused much milder changes in the ovaries of immature rats than occurred in the usual positive Aschheim-Zondek test. The ovaries while slightly lobulated (mulberry shape) were pale. Ripening follicles and poorly formed corpora lutea were usually visible, while corpora hemorrhagica, when present, required magnification. These results would be expressed as follows: Reaction I, +++ to ++++; Reaction II, 0 to +; Reaction III, + to ++. In contrast with the mild reaction of the ovaries, the uterus was enlarged and hyperemic as in estrus. The diameter of the horns often equaled or even exceeded that of the small bowel in the rat.

Representative results are collected in Table I.

Patients 1 and 2 are typical of impending abortion. Bleeding started in Patient 1 a few days after the results in the rats were known, and in Patient 2, four days after the first sample of urine was injected. Abortion followed. Abortion in the other three patients was incomplete. Three separate tests were made on the urine of the third patient, each with the modified reaction as described. An attempt to induce abortion had been made by this patient before she came to the hospital, but this was not admitted until after the third test had been completed. Without this information ectopic gestation had been considered. Sixteen days of observation,

however, between the first and second tests eliminated this possibility. The patient had bled about two months, when the last test was made and chorionepithelioma or hydatid mole had been considered, but the mildness of the ovarian reaction in each of the three tests excluded this. The diagnosis of incomplete abortion in the last two patients of the table was confirmed by operation and microscopic study. The modified reaction in the rats was the only indication of abortion. The clinical

TABLE I

NO.	METRROR-RHAGIA	CLINICAL DIAGNOSIS	ESTIMATED PERIOD OF PREGNANCY	OUTCOME PREDICTED	REMARKS
1	None	Pregnancy ?	2 mo.	Impending abortion	Bleeding started several days after the results of the rat test were known.
2	None	Pregnancy ?	1½ mo.	Impending abortion	Bleeding started the day after the rats were examined.
3	Some spotting	Ectopic pregnancy ? Abortion ?	2 mo.	Incomplete abortion	The results of three tests (4/4/34, 4/20/34, and 5/24/34) were alike. The statement of an attempted induced abortion was obtained after the last test. Patient bled continuously for six weeks while under observation.
4	2 mo.	Ectopic pregnancy ?	2½-3 mo.	Incomplete abortion	Chorionic villi were in tissues curetted from the uterus.
5	2 mo.	Right ectopic pregnancy ?	3-4 mo.	Incomplete abortion	Chorionic villi were in tissues curetted from the uterus.

history, symptoms, and physical examination of both suggested an ectopic pregnancy, but surgical operations demonstrated no changes of the fallopian tubes, and tissues obtained from the uterus by curettage contained chorionic villi.

Only one pregnancy was observed which did not abort when an "abortion" reaction was obtained. Three weeks before the test was made this patient had slight metrorrhagia, too early for her regular period. Two days after the urine was collected there was more hemorrhage, but no fetal tissues were recovered. After ten weeks she obviously was pregnant.

The end-results and the rat reactions obtained with urine from three other patients were confusing. One ended in term delivery, the second was progressing normally in pregnancy when last seen, and the third was not pregnant. The reactions in rats produced by the urine of these three women were alike, but different from either the usual "positive" Aschheim-Zondek or the modified reaction associated with abortion. The three reactions in the ovaries simulated those of the "positive" Aschheim-Zondek test, but the uterus was markedly enlarged as the "abortion" reaction. The patient who delivered at term had bled for the first two and a half months of pregnancy, and abortion was anticipated. The patient not pregnant was approaching the menopause and had not menstruated for five months.

The implication has been made that the urine of these women with abortion contained a large quantity of estrin. This view conflicts with Bland's,² who believed that estrin production diminishes with the death of the fetus. The tissue recovered from Patients 4 and 5

of the table were only small placental residues, but the urine contained much estrin judging by the hypertrophy of the uterus in the rats. The urine of Mazer and Goldstein's³ patient gave a positive estrin test after a dead fetus had been carried for four months. Jeffcoat not only considered that a large amount of estrin was present in the urine of patients with incomplete abortion but thought that the amount exceeded the anterior pituitary hormone. He concluded that estrin counterbalances the maturity producing effect of the gonad-stimulating hormone in producing the modified reactions of the ovary in patients with impending or incomplete abortion. The experiments of Leonard,⁴ Allen,⁵ and Dahlberg⁶ seem to confirm this view.

SUMMARY

1. Abortion impending or incomplete may be diagnosed by the modified reactions of the Aschheim-Zondek test in the ovaries of white female rats. These may be expressed as follows: Reaction I, +++ to ++++; Reaction II, 0 to +; Reaction III, + to ++. Accompanying these modifications is an estrous hypertrophy of the uterus.

2. All pregnant women but one, whose urine produced this reaction in routine tests, aborted.

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Urine from 51 women in the last two months of pregnancy was injected intravenously into the same number of male rabbits of approximately three months of age, from several breeds. Gross and microscopic examination of the testes removed before and after treatment gave the following results: (1) the urine injected had no appreciable effect upon the gross appearance of the testes, the seminiferous tubules, or upon the number of different kinds of germinal epithelial cells; (2) In an insignificant number of instances the treatment may have initiated or increased spermatogenetic activity; (3) The testes of animals treated with urine from women who later were found to have given birth to female children exhibited the same microscopic picture as those testes from animals which were treated with urine from women who had later given birth to male children. From these observations it is concluded that the urine from pregnant women does not offer a means of predicting the sex of the unborn child by the rabbit testis reaction.

J. THORNWELL WITHERSPOON.

PURPURA HEMORRHAGICA IN PREGNANCY

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THAT purpura hemorrhagica is infrequent in pregnancy is evidenced by the fact that up to 1925 only 47 cases had been reported in the literature. The first was that of Barnes¹ in 1867, the patient dying the day after delivery. Rushmore² in 1925 reviewed the 47 reported cases with some interesting observations. It seems more frequent in multiparas. In this series there were 32 multiparas, 7 primiparas, and 8 in whom the parity was not given. The time of its appearance is predominantly the second half of pregnancy. In Rushmore's 47 patients, 43 developed after four and one-half months; the remaining 4 in the first half of pregnancy, the earliest case appearing in the second month.

Philip Liebling³ reported one case in 1926; Hottenstein and Klingman⁴ one in 1927; in 1932 M. Palombekki⁵ one case, and G. Teasuro⁶ two cases; F. Conti⁷ one case; and P. Henriets⁸ one case, in 1933. Of these seven cases three terminated fatally.

The case here reported occurred on the Obstetrical Service of the Roper Hospital, May, 1934.

Mary B., Case 76095, a colored woman thirty-five years of age, was admitted on May 11, 1934. Her chief complaint was bleeding.

On the morning of the day of admission the patient began to have bleeding from her mouth (spitting bright red blood) and to "feel bad all over." She had dark spots before her eyes and dull pain in the lower part of her abdomen. About 1 P.M. she noted vaginal bleeding. She called a doctor but left for the hospital before his arrival, and had a sudden gush of bright red blood from the vagina as she was leaving home. Bleeding continued, but was less profuse at the time of admission than before. She vomited greenish fluid several times during the day, with no appearance of blood. The patient was pregnant, approaching full term, her last menstrual period having occurred in August, 1933. This pregnancy, her ninth, had been subjectively normal, as were all her other pregnancies. She had had seven living children and one stillbirth.

The patient was a well-nourished negress, in mild degree of shock. Her temperature was 99.8° F., pulse 116, weak and of poor volume. The blood pressure was 106/80. She had a small laceration of the mucous membrane of the tongue; gravid uterus about the ninth month, in a state of hypertonic muscular tension, without rhythmic contractions; and signs of continuous bleeding from the mouth and the vagina. The bleeding from the mouth did not appear to be due to the small laceration. Fetal heart sounds could not be heard. A catheterized specimen of urine contained a large amount of blood, grossly evident.

Expectoration of blood-tinged saliva, and vaginal bleeding with some spurts of bright red blood, continued until the day after admission. Vomiting recurred. Bleeding diminished about fifteen hours after she was admitted. At this time (7:30 A.M. on May 12) the patient complained of labor pains, but the rhythm of uterine contractions was masked by the tonic state of the uterus. The morning after admission she was delivered of a full-term, stillborn male infant. The placenta,

which was delivered intact, was of a leathery consistency. Moderate bleeding followed delivery. No further abnormal bleeding occurred during that day nor subsequently. The patient's later course was uneventful, but for a continued state of anemia. No subjective symptoms referable to this were encountered, nor any referable to nephritis or renal insufficiency. She was discharged on June 16, 1934.

Treatment.—At 5:15 P.M. on May 11, thirty minutes after admission, 2 c.c. of horse serum were administered intramuscularly, followed thirty minutes later by an additional 10 c.c. This was followed by 500 c.c. of 10 per cent glucose intravenously. At 10:15 P.M. (within six hours after admission), with bleeding continuing, an x-ray treatment was given. At 11:45 P.M. 10 c.c. of antivenin were administered. Morphine and atropine were given before delivery, and pituitrin after the third stage. On the day of delivery a transfusion of 440 c.c. of whole blood was given. The other medications consisted in ergot, postpartum; iron with copper and arsenic; and sodium perborate as mouth wash.

Laboratory Findings.—These consisted notably in hematuria, thrombocytopenia, changes in the erythrocytes characterizing a moderately hypochromic and microcytic anemia, and temporary retention of nitrogen. Smears from the mouth showed fusiform bacilli and spirochetes of Vincent.

TABLE I. LABORATORY FINDINGS IN PURPURA HEMORRHAGICA (CASE 76095)

DATE	5/11/34	5/12/34	5/13/34	5/16/34	6/7/34	11/15/34
Platelets	33,000	52,000 (12 hours after ir- radiation of spleen)	246,000 (18 hours aft- er transfu- sion. 36 hours after irradiation)	194,000	130,000	237,000
Bleeding time	More than 30 minutes. (Bleeding stopped by pressure at 30 min.)	20 minutes				
Coagulation time	5½ minutes	5 minutes				
Hemoglobin	84%	43%		43%		67%
Erythrocytes				2.72 million		4.79 million
Reticulo- cytes					6%	
Total leuco- cytes	21,000		6,350		3,800	
Polymorpho- nuclears	72%		82%		70%	

In addition to these characteristic features of thrombocytopenic purpura, our case manifested bleeding into the urinary tract, which is apparently rare. On admission a catheterized specimen of urine contained a large amount of blood, too large for the significant interpretation of other findings in that specimen. The next catheterized specimen, obtained six days later, contained only a few blood cells on microscopic examination. At this time, five days after delivery and after the cessation of spontaneous bleeding, with no signs or symptoms to suggest renal failure, a blood chemical analysis showed marked nitrogen retention, the urea nitrogen being 152 mg., the creatinine 20.4 mg., figures which, in a chronic case of renal insufficiency with nitrogen retention, would foretell a certain and early fatal termination. Successive

blood chemical analysis showed steadily decreasing urea nitrogen and creatinine, the figures sixteen days later (June 4) being 66 mg. for urea nitrogen and 5 for creatinine, and continuing to fall. A phenolsulphonephthalein kidney function test at this time (June 8) showed first hour excretion 5 per cent, second hour 2½ per cent. Before discharge from the hospital, five weeks after admission, the urea nitrogen was 29 and kidney function by urea clearance test was 13 per cent of normal. Her apparent tendency to steady improvement was further demonstrated by a kidney function test (urea clearance) made on November 15, five months after the previous one, showing that the blood urea nitrogen had reached the upper normal level of 18 mg., although the clearance was still below normal, being 30 per cent. A search of the literature has revealed only five patients in whom hematuria was noted; of these, four died and records of autopsies are available on two. In only one case⁶ were the findings and pathology described such as we believe to be illustrated by our case. In the case reported by Tesauro⁶ death resulted from intracranial hemorrhage, and autopsy revealed also the fact that the capsules of the kidney glomeruli were filled with blood. Such a lesion would account for retention of nitrogenous products by mechanical interference with glomerular function, without necessarily inflicting permanent injury upon the glomerular tissue.

Adding to the 44 cases previously reported the 8 here collected in which the final results are known, we have a total of 52 cases with 29 deaths, a mortality of 55.7 per cent.

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Schmid transplanted uterine mucosa into the vaginal wall, thus producing an artificial endometriosis since all of the transplants grew. The author did this in 19 women and produced a regular menstruation with external discharge in all. This makes it possible to produce regular menstruation in young women with functioning ovaries even after the uterus has been removed. The value of this procedure is entirely psychic but can be used to prevent the psychic depressions which are found in many young women who have undergone hysterectomy.

RALPH A. REIS.

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The author collected 359 cases of rectouterine endometriosis from the world literature and from his analysis concludes that radical surgery is not only dangerous but also unsatisfactory in that much diseased tissue is left in situ. Since endometriosis is directly dependant upon ovarian function, simple ovarian destruction is sufficient. This may be accomplished by bilateral ovarian extirpation but can be done in a simpler and safer manner by radiation, either with radium or x-ray. All that is necessary to cure this condition is the production of an artificial menopause.

RALPH A. REIS.

TWIN PREGNANCY WITH ONE LIVING FULL-TERM CHILD AND ONE FETUS PAPYRACEOUS

P. K. EDMUNDS, M.D., LOS ANGELES, CALIF.

MRS. M. B., Mexican, aged twenty-four, was admitted to Golden State Hospital Sept. 30, 1933, in labor. Married three years, the patient had a living male child apparently normal in every respect. The present gestation dated to the last menstrual period Dec. 23, 1932, prior to which time the menses had been quite regular except for occasional irregularity in the form of prolonged intermenstrual periods since the birth of the first child. Before the first pregnancy her menses had been regular, of the twenty-eight-day type, lasting four days, and not painful. There had been no miscarriages. During the first six or seven weeks of the latter pregnancy the patient had experienced dull dragging pain in the right upper quadrant of the abdomen and in the right flank. She had noted in the latter months of gestation absence of the feeling of fullness in the pelvic region which she had noted with the first child. She had attended the prenatal clinic for the first time ten days before coming to this hospital. On this occasion she was not informed of any unusual findings on examination if such had been encountered. Pains had begun at 11 A.M. on Sept. 29, 1933, were not severe, and occurred every ten to twelve minutes.

The general physical condition was good. The abdomen was slightly pendulous, flaccid, and presented striae but no scars. There was about 5 cm. diastasis present. The ovoid was in the oblique, the diagonal running from the left upper quadrant to the right lower quadrant. The fetal back was toward the left side of the abdomen, the small parts were felt anterolaterally on the right side. No head was palpated in the pelvic region but it was indefinitely felt in the left upper quadrant where ballottement was elicited. The fetal heart tones were heard most distinctly to the left of the umbilicus and were 140. A diagnosis of breech presentation was made, and this was confirmed by rectal examination when the presenting part was felt high up in the pelvis and from its contour was taken to be a foot. The cervix was moderately effaced, dilated about 5 cm. and the bag of waters was intact. Preparations were made for delivery anticipating extraction of a breech-footling presentation. Before preparations were complete, the bag of waters ruptured and a large volume of liquor escaped. Soon thereafter, pains became frequent and severe and within a relatively short interval the presenting part was visible at the outlet, and on examination, proved to be a knee. The patient was anesthetized with ether and the child was extracted without difficulty. It was a male weighing 7 pounds, 3 ounces, apparently normal in every respect. The placenta separated spontaneously within ten minutes, whereupon the upper border of the uterus was palpated and presented the characteristic (hatchet) shape except in the right cornual region where a rather firm tumor mass was noted. On downward pressure over this area the placenta was delivered and thereafter the uterus was felt to be in the midline, of uniform outline and contracted. Hemorrhage was not unusual and there were no tears. Of unusual interest was a firm flattened mass inclosed in a sac on the maternal surface of the placenta and which was the first visible part of the placental mass as the latter was delivered. Through the sac the flattened mass appeared gray white in color, was about as long as the hand

from wrist to the tips of fingers, firm to hard in consistency, nonadherent to the placenta and unquestionably of fetal form. Over what was taken to be the head a small opening was made in the membranes and the fetus was expressed. The latter measured 14.5 cm. from crown to perineum and was compressed from side to side, the head symmetrically, the trunk with the (adherent) extremities, obliquely. The extremities were in a flexed attitude and fixed to the trunk by a covering of firm vernix caseosa. The ribs of the left chest wall were visible and palpable and the whole mass was firm to hard in consistency. The sac contained only a small amount of fluid and was separated from the other sac which had contained the normal fetus, by a septum made up of two layers only. On closer inspection of the dead fetus a scrotal sac was found which led to the conclusion that this was a case of monozygotic twins. The placenta was of average size, measuring 16 cm. in diameter, 13 cm. in thickness, and was of normal appearance

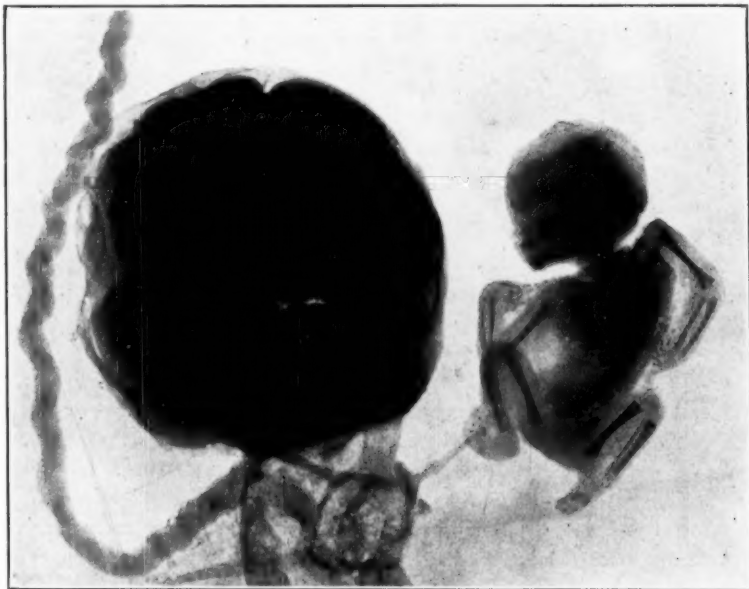


Fig. 1.—Photographic reproduction of x-ray of fetus papyraceous shortly after delivery showing the well-developed skeleton; also the comparative sizes of the two umbilical cords.

and consistency on both the maternal and fetal sides. There were two separate cords, the vessels of which anastomosed at the (marginal) insertion into the placenta. That of the living fetus was of average length and measured about 1.5 to 2.0 cm. in diameter. The cord of the dead fetus measured 0.5 to 0.75 cm. in diameter, and but 13.5 cm. from the placenta to the perineal region where the cord disappeared beneath the firm caseous matter which covered the trunk and extremities of the fetus. An effort was made to dissect out the vessels of both cords and to determine their interrelationship at their insertion into the placenta. It was found that arteries anastomosed with arteries, veins with veins, and there was no arteriovenous anastomosis of the larger vessels. The vessels of the cord of the dead fetus were further dissected out for the entire length of the free part of the cord, and from this point on it was possible to liberate and follow the cord. It coursed upward beneath the left thigh, the left forearm, around the neck of the fetus, and back beneath the ascending loop to the navel. In its course about the

neck of the fetus it lay in a trough-like groove. One lower extremity was dissected free and measured from thigh to knee 5 cm. and from knee to the tip of the toes 6.5 cm., the total length of the fetus approximating 25 cm. from crown to heel or about the length of the fetus in the fifth month of development. On x-ray examination the bony skeleton was found to be well developed (Fig. 1).

It is probable that in this case death of the fetus resulted from strangulation due to the cord around the neck.

SUPRARENAL CORTEX THERAPY IN PERNICIOUS VOMITING OF PREGNANCY

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THE purpose of presenting at this time a single case report in a subject of this kind is not an attempt to draw any conclusions, but rather a desire to stimulate obstetricians to try this form of therapy. If, as is indicated in this one case, adrenal cortex proves successful in overcoming even a few of the types of obstetric vomiting, a great advance will be accomplished.

Kemp,^{1, 2} reported the use of adrenal cortex in 16 of his obstetric patients who were troubled with more or less mild attacks of vomiting. All but one were in the first trimester. Kemp believed that normal pregnancy was characterized by a hyperfunction of the adrenal cortex inasmuch as it was frequently found hypertrophied. He further believed that adrenal cortex insufficiency resulted in gastrointestinal disturbances of which vomiting was a prominent symptom. He therefore reasoned that some women vomited during pregnancy because their adrenal cortex did not pick up enough added function necessary for the condition. Whatever the rationale of this hypothesis proves to be, Kemp obtained complete and almost immediate freedom from vomiting in all of his treated patients. Not one of Kemp's patients had ketosis nor did any show symptoms as severe and dangerous as in our patient.

Our interest in Kemp's work was stimulated by the fact that our patient derived no relief from the conventional endocrine or other therapeutic agents. In spite of the intensive treatment accorded her for ten days in the hospital she continued to lose ground and rapidly developed such a dangerous condition that surgical intervention was indicated. Therapeutic abortion would not be sanctioned by her church. It was then decided to try intravenous suprarenal cortex (Armour's). With this medication the patient rapidly changed from a state bordering on ketotic coma to her present condition, in which she walks, eats normally, and has regained the 27 pounds lost during her stormy siege.

Mrs. B. D., aged twenty-seven, white. Appendix removed in 1926 and she had a uterine suspension in 1927. She began to menstruate at thirteen years of age, every twenty-six days for five days, the amount of which was moderate, but with severe pain. She had always been regular and had no leucorrhea. Her last period was June 8 to 13, 1934. She was married June 9, 1934. On July 21, 1934, she reported to one of us (J. M.) that she had severe nausea with persistent vomiting. She was sent home and put to bed and the conventional routine prescribed. In addition, the patient received hypodermically 2 ampoules of corpus lutein per day. This seemed

to increase her nausea and vomiting so at the end of five days it was discontinued. She was then given $\frac{1}{2}$ gr. of thyroid (Burroughs Wellcome & Co.) q.i.d. with no improvement.

She was admitted to the Worcester Hahnemann Hospital too weak to walk. The urine showed a very marked trace of acetone and diacetic acid but no sugar. She was given 5 per cent glucose-saline solution intravenously in 1,000 c.c. doses twice on this day. Her temperature, pulse and respiration rates were 98.2°, 86, and 18. Although she took only small amounts of water by mouth, she frequently vomited large amounts of a thin, greenish-yellow fluid.

She continued to receive the intravenous therapy daily (2,000 c.c. each twenty-four hours) for the following eight days during which acetone and diacetic acid increased. She continued to vomit large amounts of fluid although only small amounts of cracked ice and tart fruit juices were taken. Even the intravenous therapy began to bring on attacks of vomiting.

She was then started on 90 gr. of bicarbonates by mouth in small divided doses. At first this made her feel better. She continued to vomit, but in lesser amounts. She still received the intravenous therapy of glucose-saline solution. As the nausea and vomiting continued the alkalies were administered rectally.

She became flushed and drowsy; there was a marked odor of acetone on her breath and a glassy stare in her eyes. At noon on that day she was given another 1,000 c.c. of glucose-saline solution intravenously to which was added, for the first time, five units of insulin. Two hours later her blood sugar was 105 mg., but there was 2 per cent sugar in her urine specimen. She was then given her first injection of an entire ampoule of suprarenal cortex (Armour's) intramuscularly. She received two more such injections of adrenal cortex during the remainder of that day. That night she was given intravenously 500 c.c. of a 10 per cent glucose-saline to which was added 20 units of insulin. The next day she reported that after the previous night's intravenous medication she had felt as if she were floating in air for a few minutes.

The following day she was again given 3 doses of the suprarenal cortex, but no insulin or glucose-saline. Although she still felt nauseated and vomited frequently, her vomitus now began to be in negligible amounts. She retained small amounts of cracked ice and tart fruit juices by mouth.

She continued to improve rapidly for the following three days, although she received only two more intravenous injections of a 10 per cent glucose-saline solution in 500 c.c. doses to which was added 30 units of insulin. These continued to make her nauseated and vomit.

At this time her general improvement was so marked that her bed was wheeled out on the sun porch. She continued to take and retain 90 gr. of bicarbonates orally. During this interval her urine showed a gradually diminishing concentration of acetone and diacetic acid, and on this day the test for diacetic acid was negative for the first time.

She began to eat and retain a fat-free diet. Her vomiting ceased entirely although her nausea was a bit more stubborn. On the thirty-first of August her urine was acetone-free for the first time. All medication had been discontinued except the intravenous adrenal cortex which she continued to get three times daily. On this day she was allowed out of bed for ten minutes. She was weighed and found to have lost 27 pounds.

She continued to regain her appetite and strength rapidly. On the second of September (ten days after the first suprarenal cortex injection) she was strong enough to go home. On this day the intravenous route was discontinued and replaced by

Armour's suprarenal cortex tablets, grains iii, three times daily. Her temperature, pulse, and respiration rates did not vary materially from those on her admission.

At present (October 8) she is at home. She eats her food ravenously, has lost all traces of nausea and continues to take adrenal cortex tablets faithfully. She now weighs 130 pounds. She has not aborted.*

DISCUSSION

One may argue that insulin was used for the first time on the same day that the suprarenal cortex injections were started and that the insulin was the cause of her improvement. However, the intravenous glucose-saline-insulin injections made her sick and were, therefore, discontinued before her urine ketosis was cleared. She did not receive any insulin-glucose-saline solution for four days before her urine became acetone-free. Also, one may argue that her vomiting would have ceased spontaneously at the end of her first trimester, but she was still in her second month of pregnancy. Moreover, ketosis is a vicious cycle and is, therefore, not cleared spontaneously.

We are using it in all forms of vomiting in pregnancy and hope to publish our results as soon as our series of cases is sufficiently large. We are also using this therapy in all other forms of vomiting.

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THE TREATMENT OF PRURITUS VULVAE WITH SUBCUTANEOUS ALCOHOL INJECTIONS

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THE therapy of pruritus vulvae in patients having other vaginal complicating factors is directed toward the eradication of the underlying condition, and all constitutional diseases must be adequately treated. In all other cases, in which no definite etiologic cause is apparent, we have found the use of perivulvar alcohol injections of great value. Such patients have usually been suffering from pruritus for a long time, and have in most instances run the gamut of local treatment, including all kinds of soothing, cooling, or anesthetic solutions or salves. Many have previously had local cautery or x-ray treatment without relief. Even surgery has been utilized occasionally. In some of these patients the itching becomes so increasingly intolerable that morphine in large doses eventually becomes necessary.

*This patient was delivered of a full-term male infant on March 19, 1935, both doing well.

We are reporting in this paper the results obtained in a series of fifteen cases of pruritus vulvae, treated by subcutaneous alcohol injections. The technic of the injection varied somewhat in different cases.

TECHNIC

As a preliminary measure, the vulva and mons veneris were shaved and cleansed, and the limits of the pruritic area marked out. The cutaneous nerve supply of the external genitals is derived from the hypogastric branch of the iliohypogastric, the inguinal branch of the ilio-inguinal, and the perineal branch of the pudic nerve. The dorsal nerve of the clitoris is also a branch of the pudic nerve. All of these nerves, except the dorsal nerve of the clitoris, penetrate the deeper structures at the outer margin of the vulva and are distributed toward the midline. Since the superficial nerve supply radiates to the midline, it suffices to inject the periphery of the pruritic area in order to cut off sensation. A separate injection is made to eliminate sensation in the dorsal nerve of the clitoris.

Under gas-oxygen anesthesia, 95 per cent ethyl alcohol is injected completely around the margin of the pruritic area. The injections may be spaced about one-quarter inch apart, a drop or two being instilled at each point as advocated by Stone in the treatment of pruritus ani,¹ or made as a continuous infiltration along the outer border of the vulva. The area about the clitoris is separately injected along either side of the prepuce. From 10 to 20 c.c. are required for the complete operation. More alcohol will be required for continuous infiltration than for spot injection. At the present time I personally prefer the spaced spot injections, as I believe that they accomplish the same purpose, use less alcohol, and are followed by less local reaction. Special care must be taken not to inject under the vaginal mucosa, as extensive sloughing may ensue. A reactionary swelling of the labia always appears soon after the injection. This can be partly controlled by hot applications of boric acid or Burrow's solution. The patient may be allowed out of bed in twenty-four to forty-eight hours.

RESULTS

In our series of fifteen patients all but two were married. The youngest was thirty and the oldest sixty-five years. Ten had had children. The duration of the itching had varied from two months to thirteen years, the average length of time being 3.7 years. Three patients had a moderate or profuse vaginal discharge. The external genitals, particularly the labia, showed evidences of scratching, excoriation, redness, and thickening. In one patient there was marked tanning and in another atrophy of the labia as a result of x-ray treatment. In twelve patients the cervix was entirely normal; one was slightly eroded and two showed nabothian cysts. The latter two patients also had profuse cervical leucorrhea. Perhaps they should not have been included in this series, inasmuch as a possible local cause for the pruritus was present. The urine and blood examination of all patients was negative. All fifteen patients had had previous medical attention. Four had novocaine injections, two had superficial cauterization, two had x-ray therapy, and one, in addition to other treatment, failed to get any relief from several grains of morphine each day.

In all fifteen patients, relief from the itching was experienced immediately after the injection, and in only three was there marked swelling after the alcohol injection. In four cases no late follow-up was possible. In the other eleven the duration of relief varied. In one of the two patients with inflammatory cervical involvement the relief lasted but a few days and then the itching partially returned. It was severe

around the clitoris and at the fourchet, but practically absent around the labia. In the other patient with inflammatory cervical disease the relief lasted for one month. Both of these patients are under treatment for the endocervicitis. In another case relief was transitory. This patient subsequently was given electrocoagulation of the vulva for leucoplakic kraurosis. In one patient relief after the first injection lasted two months. Nine months have elapsed since the second injection, and there is still no recurrence of the itching. In one patient injected three times, the intervals of freedom from itching were three months, four months, and now three years. In another patient injected eight times, the intervals of freedom were two months, two months, four months, four months, two years, one year, two years, and now two years. Excluding the first three patients mentioned, in whom relief was obtained for only a few days to one month, the shortest period of relief was two months, the longest four years. The average period of relief was 13.6 months. If we include these three cases, the average period of relief was 11.7 months. In four patients the itching has not recurred to date. The interval in these patients is nine months, fourteen months, three years, and four years.

Alcohol injection for pruritus vulvae of unknown origin affords prompt relief from itching. Even though recurrence of symptoms may subsequently take place, the procedure is well worth while for the complete comfort it brings about in the free interval, and it can be repeated as often as necessary.

This method of treatment should be more extensively utilized, and be given preference to less effective or more drastic remedial measures.

I am indebted to Dr. Walter T. Dannreuther, Director of the Department of Gynecology, for permission to include his personal cases in this paper.

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151 WEST 77 STREET

FULL-TERM PREGNANCY COMPLICATED BY RUPTURED SPLENIC ANEURYSM

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ANEURYSMS of the splenic artery are unusually rare. Since pathognomonic signs of splenic aneurysms are absent, the diagnosis is usually not made until rupture occurs. This is especially true, when it is associated with pregnancy.

A study of splenic aneurysms made by Schroeder¹ showed, that of 32,768 autopsies performed in Europe, only twenty cases of splenic aneurysms were included. It is of interest to note, however, that of the fifteen case reports reviewed by Lower and Farrell,² three cases were associated with pregnancy. One of these was reported by Saenger³ in an eight months' pregnancy. The patient was suddenly seized with abdominal pain, followed shortly by collapse. On exploration, free blood was found in the peritoneal cavity, which led to the discovery of a ruptured splenic aneurysm.

The second case was described by Lundwall and Gödl,⁴ in which a ruptured aneurysm occurred during the ninth month of pregnancy. Because of bleeding in the abdominal cavity, a supravaginal hysterectomy was done; however, the source of bleeding was not discovered until after the patient died. An autopsy revealed a ruptured aneurysm of the splenic artery.

The third case was reported by Smith,⁵ which occurred in a negress, who entered the hospital in shock, with the diagnosis of a ruptured ectopic pregnancy. During laparotomy free blood was found in the lesser peritoneal cavity and further examination showed a ruptured splenic aneurysm. Although bleeding was controlled with tampons, the patient died two hours later.

The following case is presented, because of the rarity of this condition, and the difficulty in making a diagnosis, particularly when complicating a full-term pregnancy.

CASE REPORT

Mrs. R. O'G., a white multipara (para iii), thirty years of age, had been under our obstetric care for her two previous pregnancies, and was delivered uneventfully. She came under observation for her third pregnancy at the end of the second month of gestation. The first day of her last menstrual period was on June 22, 1933. She was seen at regular intervals for the balance of her pregnancy, during which time no abnormal findings were elicited. Her blood pressure varied from 100/60 to 128/82. At times a trace of albumin was noted in the urine. There was a systolic murmur at the apex, transmitted to the axilla.

The patient was last seen at the office on March 31, 1934. On April 1, 1934, at 3:30 A.M., she was suddenly awakened with severe pain in the epigastrium, accompanied by vomiting and pain in the right shoulder. She was advised to enter the hospital immediately. On admission at 6:35 A.M., she stated that she felt somewhat better, but still had pain in the upper left abdomen and right shoulder.

Examination at this time revealed the patient acutely ill, not in labor, but with a pinched face, cyanosis of lips, and shallow breathing. The temperature was 98.4° F., the pulse was 88 and regular. The blood pressure was 114/82. The uterus was enlarged to the size of a full-term pregnancy. The abdomen was slightly tender throughout, but more marked in the epigastrium, with moderate rigidity. The uterus was not contracting. The rectal examination showed no dilatation, cephalic presentation and a minus two station. The blood count showed 4,100,000 red cells, 18,300 white, 55 per cent hemoglobin (Sahli) with slight anisocytosis and poikilocytosis. The differential count showed: polymorphonuclear cells 90 per cent, small lymphocytes 6 per cent, large lymphocytes 3 per cent, and one transitional cell. The urine examination was negative.

A diagnosis of a ruptured viscus was suspected and she was kept under very careful observation. Repeated blood examinations showed no marked changes from the first examination. The pulse fluctuated from 72 to 96.

At 8:30 P.M., the patient attempted to leave the bed and she experienced again severe pain in the epigastrium and left shoulder blade. This was associated with dyspnea, cyanosis, nausea, and vomiting. The pulse became rapid and irregular. The fetal heart tones were 144 and regular. A diagnosis of intraabdominal bleeding was made. An injection of 1,000 c.c. of 5 per cent glucose in saline was started intravenously and an exploratory laparotomy performed. The peritoneal cavity was found to be full of blood. A low cervical cesarean section was done, and a live baby girl of seven and a half pounds was delivered. The abdomen was then explored for the source of bleeding.

Exploration revealed a large mass in the epigastrium, in the region of the lesser omental cavity. Meanwhile, the patient's condition became very grave. The pulse was about 170 and imperceptible at times. Because of her poor condition, the abdomen was closed rapidly. A blood transfusion of 570 c.c. of blood was given by the Scannell method. During the transfusion, a moderate improvement of the patient was noted, and the pulse became slow and regular. However, five minutes after the transfusion was completed, she again complained of severe pain in the

epigastrium and right shoulder. This was associated with a marked pallor, and the pulse became imperceptible. She died a few minutes later.

Autopsy.—The abdominal cavity was filled with free blood. There was a large clot in the lesser omental cavity. The hemorrhagic area extended into the retro-peritoneal spaces. The foramen of Winslow was open. The gallbladder was small and contained no stones. The uterus was contracted and extended just below the umbilicus. Both kidneys were of normal size. There was no rupture into the pedicle. The splenic artery as it transversed about the middle portion of the pancreas presented a ruptured dilatation about 15 mm. in diameter. The kidneys, liver, and spleen were pale. The adrenals showed no hemorrhages. The tubes and ovaries were enlarged, but showed no pathology.

Anatomical Diagnosis.—Ruptured aneurysm of the splenic artery at the bifurcation, prepancreatic hematoma, old and recent blood clots in greater peritoneal cavity, and acute anemia of all organs.

Microscopic examination showed the splenic artery slightly sclerosed in the media. The aneurysm was probably of a congenital origin.

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3460 LAWRENCE AVENUE

ABRUPTIO PLACENTAE COMPLICATING TWIN PREGNANCY

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ABRUPTIO placenta is always a serious condition. Its presence in twin pregnancy greatly endangers three lives. The maternal fatalities, according to available statistics, range from 2.6 to 66 per cent, while the fetal mortality varies from 60 to 95 per cent. The present case of abruptio placenta complicated a bioval twin pregnancy near term, with hemorrhage, treated by cesarean section, with recovery of the mother and one child.

L. M. G., white, school-teacher, aged twenty-six, primipara, near term, entered the hospital, March 10, 1934, because of vaginal spotting and pain in the right lower quadrant of the abdomen. She had been married for a year and four months, and had an abortion two and a half months after marriage. The past and family history was essentially negative. Menstrual history normal. The probable date of confinement was March 28, 1934. She received prenatal care elsewhere. She reached the ninth month of pregnancy without any evidence of toxemia or any other complication. There had been no edema or headache. She was admitted at 1:00 P.M. and was placed under close observation. At 4:00 A.M. next morning, I was hurriedly called because of profuse bleeding. She was very pale and complained of pain in the lower abdomen. The abdomen was greatly enlarged and its walls quite rigid. The uterus was also abnormally large, tense and rigid. There were no uterine con-

tractions. The fetal parts and heart tones could not be obtained. There was marked tenderness in the right lower quadrant and moderate vaginal bleeding. The vagina contained many clots. Rectal examination revealed the cervix hard, high and barely admitting the tip of the index finger. The head was not engaged. The blood pressure was 100/68, temperature 98° F., pulse 120, and respirations 30. Urinalysis was negative. Hb 60 per cent (Dare). Red blood cells 3,828,000. Coagulation time (Bogg) three minutes. Wassermann was negative. A diagnosis was made of abruptio placentae with severe internal and moderate external hemorrhage with intrauterine death of the fetus. One thousand cubic centimeters of 10 per cent glucose were given intravenously and $\frac{1}{6}$ gr. of morphine by hypodermic injection. She was transferred to the operating room and a classical cesarean section performed. After incision of the uterus a twin pregnancy was revealed. The first placenta was completely separated from the uterine wall by large, dark clots and fluid blood. A stillborn female ($3\frac{1}{2}$ pounds) was delivered. The second child, also a female, was living and weighed 6 pounds and 4 ounces. The placenta which was well attached was manually removed. It was normal in appearance, but smaller than usual. The detached placenta was very small. It weighed 8 ounces. It showed an acute brownish red infarct on the maternal surface. The consistency of the infarct was more homogeneous and slightly firmer than the surrounding normal placenta. Microscopically it revealed dilated, engorged, and occasionally ruptured capillaries and veins in the villi. There was also severe necrosis of the syncytium, Langhans layer and the stroma, and absence of the intervillous hyaline substance.

The patient had a rapid and uneventful recovery. She was discharged on the sixteenth day in fine condition. The baby gained in weight during the stay in the hospital.

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Among 2,000 women delivered in the Institute of Obstetrics and Gynecology of Torino, 20 were cardiopathies. They fall into the following groups: (1) Patients at term or in last months of pregnancy, cardiac disease well compensated, slightly or badly decompensated. (2) Cardiopathic pregnancy in the first months of gestation.

Of 73 pregnancies in these 20 women 12 (16.7 per cent) ended in abortion, either spontaneously or artificially; 47 (64.3 per cent), reached term; and 14 (19 per cent) ended prematurely. Of the 47 babies born at term, 5 (10.6 per cent) died at birth or a few days later, and also 2 of the 14 premature babies.

In his opinion the maternal prognosis is good for the majority of the cardiopathic cases in pregnancy. The author places more importance on the functional capacity than anatomic lesion of the heart. In rare cases with grave decompensation early pregnancy is interrupted. In all other cases it should be attempted to carry pregnancy to full term. Labor in most cases is spontaneous.

The fetal prognosis is good for the newborn at term in well compensated cases. Prognosis is doubtful for premature infant or in instances of grave cardiopathy.

AUGUST F. DARO.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

COMPARABILITY OF MATERNAL MORTALITY RATES IN THE UNITED STATES AND CERTAIN FOREIGN COUNTRIES

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THE claim has been made frequently that the maternal mortality rates in the United States should not be compared with those of other countries, that the methods of assignment of maternal deaths were so different that it was unfair to the United States to make this comparison, and that were comparability possible, the United States would not stand so high as it does in the list of nations. Therefore we welcome the study that has just been published by the Children's Bureau on the "Comparability of Maternal Mortality Rates in the United States and Certain Foreign Countries." This was initiated by a subcommittee of the Committee on Prenatal and Maternal Care of the White House Conference on Child Health and Protection. Dr. Tandy, Director of the Statistical Division of the Children's Bureau, was in charge of the investigation and wrote the report.

In order to obtain data that would throw light upon the effect of the differences in assignment procedure upon the comparability of maternal mortality rates, 1,073 United States death certificates on which pregnancy or childbirth was mentioned were chosen for study. These deaths occurred in 1927 and the certificates were chosen at random but represented every type of puerperal death. In this list there were many that were identical or very similar, and for transmittal to the foreign countries 477 certificates were carefully selected so as to include at least one death from every type in the sample. These 477 certificates were set up in a list form showing the primary and contributory cause of death, performance or nonperformance of operation or of an autopsy. Two blank spaces were provided, and it was asked of the foreign countries that the first of these columns be checked if the death could be classed as puerperal, and the second if it would be classed as nonpuerperal by the statistical bureau in charge of coding cause of death in each country. No information was given in these certificates in regard to the cause assigned in the United States.

These lists were sent to 24 foreign countries and answers were returned by the following 16: Australia, Canada, Chile, Czechoslovakia, Denmark, England and Wales, Esthonia, France, Irish Free State, Italy, Netherlands, New Zealand, Northern Ireland, Norway, Scotland, and Sweden. After these lists had been returned, the 596 deaths in the original group not sent abroad but identical with those that were sent, were classed as puerperal or nonpuerperal in accordance with the assignments made by the foreign countries for those that had been transmitted. The groups of deaths were then thrown together and a tabulation of the 1,073 certificates was prepared showing the assignment of the United States Bureau of the Census and the classification as puerperal or nonpuerperal by each of the foreign bureaus that complied with the request.

Some very interesting facts were obtained from this classification. The United States assigned to the puerperal state 92.9 per cent of the 1,073 deaths associated with pregnancy and childbirth. Denmark alone would have assigned more deaths than the United States. She would have classified 99.4 per cent as puerperal. Norway would have assigned the fewest, 76.9 per cent. England and Wales came next to Norway with 78.7 per cent. The United States assigned to the nonpuerperal causes 7.1 per cent, while Norway would have assigned 23.1 per cent and Denmark 0.6 per cent. Australia, the Netherlands, New Zealand, and Scotland made assignments in approximately the same ratio to puerperal and nonpuerperal causes as did the United States. This is as might be expected for the first three countries have officially adopted the United States *Manual of Joint Causes of Death* and Scotland also makes use of it although never officially adopted.

This study shows that although in some of the countries the methods of assignments to the various rubrics are similar there are real differences in procedure. In some of the countries infectious diseases resulting in high mortality are given preference to puerperal causes. In others this is not followed. The assignment of cardiac conditions varies, yet pulmonary tuberculosis is generally considered a primary cause. By most of the countries acute nephritis is regarded as another name for puerperal albuminuria and convulsions, but by some it is not so classified. There is no agreement among the countries in regard to embolism or to the large number of deaths due to abortions.

General rules for procedure are in use in the various statistical offices, but there are real differences which lead to slight alterations in the assignments, and therefore render statistics not completely comparable. Tables are given in the study showing the percentage change that would have obtained in the United States under the assignment procedure of the different countries which answered the questionnaire. The best position that the United States could have achieved would have been fifth from the highest, and under every system of assignment it is seen that the United States has a high maternal mortality rate. This study shows that we must admit our rate is high, and that within certain limitations comparability is possible. It brings out clearly, however, that our rate is falling—slowly, to be sure, but steadily—while in several of the countries the mortality rates are significantly higher, Canada alone showing a distinct drop.

Two factors: the first, differences in definitions of live births and the second, variations in the completeness of registration, are frequently mentioned when the comparability of the statistics of the United States and foreign countries is questioned. This study shows that complete unanimity in the definition of live births should prevail, and that it is essential to have complete birth registration, but even with differences which might arise from these two factors they are inadequate to explain more than a few points our maternal mortality, and we would still retain a high position in the maternal mortality rate list of nations.

In conclusion the following recommendations are made:

1. It would be desirable for the United States Bureau of the Census to publish annually a table showing deaths associated with pregnancy and childbirth by primary and contributory cause and also a table showing deaths associated with pregnancy and childbirth by states, by color, in urban and in rural districts in the states.
2. An investigation of the differences in assignment procedure and the formulation of rules uniformly acceptable to important countries should be undertaken by the International Statistical Institute at an early date.

Dr. Tandy's study is an important contribution to a more complete understanding of maternal mortality rates. It shows conclusively that the statistics of other

countries and ours cannot be compared with absolute fairness. Yet the variations are not so great that the statistics do not give investigators a clear and concise understanding of the conditions in the various countries. For years physicians and others interested in our maternal mortality rates have insisted that because of this lack of comparability, it was unfair to place the United States so high in the list. This report shows clearly, however, that even with the kindest consideration our position in the list of nations would not be materially altered.

The study is a further challenge to the medical profession to make added effort to improve the maternal mortality rate. The medical profession alone cannot accomplish this. The education of the women, and the men also, of the country must be insisted upon. Community responsibility for this condition is real, but the medical profession must be the leaders in the effort to lower the maternal mortality rate.

Peckham, C. H.: An Investigation of Some Effects of Pregnancy Noted Six Weeks and One Year After Delivery, Bull. Johns Hopkins Hosp. 54: 186, 1934.

The stillborn and neonatal mortality rates were high, even for a clinic population with a large percentage of referred emergency cases. If women would apply early for prenatal care, and after delivery would attend regularly the child welfare clinics, the rates would be lowered appreciably. The black women were more successful in nursing their babies than the whites. The percentage of nursing mothers was high. Even if the supply of breast milk was insufficient ten to fourteen days after delivery, it often became adequate later. The incidence of perineal tears, relaxed vaginal outlets, cervical tears, and subinvolution of the uterus were greater in the white than in the black race. The ultimate result to the perineum in a series of cases not treated by routine episiotomy was good, only 1.31 per cent of the primiparas being left with marked relaxations. Probably as a result of too rapid resumption of household duties 10 per cent of the primiparas and 12 per cent of the multiparas had definite subinvolution six weeks after delivery. About a sixth of the total number of patients had retroflexed uteri a year after delivery. The earlier in the puerperium an attempt is made to correct this abnormality the greater are the chances for success. Only 8.37 per cent, including multiparas, were left with faulty abdominal support as evidenced by diastasis of the recti muscles.

In 71.45 per cent of the cases menstruation recurred before the cessation of lactation. A fourth of the white patients and a third of the blacks again became pregnant in the first year after delivery. In only 2.77 per cent of the primiparas and 7.15 per cent of the multiparas was it felt that the child-bearing had had a deleterious effect. This is a very low figure in consideration of the social and economic environment of this class of patients.

C. O. MALAND.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF OCTOBER 9, 1934

The following papers were presented:

The Operative Treatment of Sterility. Dr. Francis W. Sovak. This paper is a part of the chapter on the operative treatment of sterility contributed to the *Textbook of Gynecology*, edited by Carl Henry Davis.

Discussed by Drs. I. Rubin, Wm. H. Cary and E. A. Bullard.

Two Years' Experience With Theelin Treatment of Gonorrheal Vaginitis. Dr. James R. Miller. (For original article see page 553.)

This paper was discussed by Dr. R. M. Lewis.

BROOKLYN GYNECOLOGICAL SOCIETY

MEETING OF OCTOBER 5, 1934

The following papers and discussions were presented:

When to Operate in Ruptured Ectopic Gestation. Dr. W. C. Meagher. (For original article see page 541.)

Discussion by Drs. H. M. Mills, T. S. Welton, S. A. Wolfe, C. A. Gordon, S. B. Schenek, L. S. Schwartz, and J. A. Driscoll.

The Management of Prolapse of the Uterus. Dr. C. A. Gordon. (For original article see page 547.)

Discussion by Drs. Cameron Duncan and A. Koplowitz.

Vogt-Möller, P.: Treatment of Sterility and Habitual Abortion with Wheat-Germ and Wheat-Germ Oil (Vitamin E), *Acta obst. et gynec. Scandinav.* **13:** 219, 1934.

A report is presented by Vogt-Möller of 25 cases of barrenness in women, especially habitual abortion (20 cases) and sterility (5 cases), which were treated with wheat-germ oil or (and) with wheat-germ (vitamin E). The results obtained in habitual abortion are particularly favorable since the birth of a living child was attained in 17 out of 20 cases.

J. P. GREENHILL.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Diseases of Respiratory and Circulatory Systems and Intestinal Tract Complicating Pregnancy

Maniscalco, S.: Bronchial Asthma and Pregnancy, *Monitore Ostet.-Ginec.* 4: 376, 1933.

The author presents a case of bronchial asthma which started at the second month of the fifth pregnancy of a woman thirty-six years old. History was absolutely negative to allergic conditions and respiratory infections. She had no history of childhood diseases except the typical winter colds. At the age of twenty-two, during a severe influenza epidemic, she had a bronchopneumonia with a high temperature for nine days. After ten years she was again stricken with a less severe bronchopneumonia. Three years later she had a third attack of moderately severe bronchopneumonia, recovery taking about three months. The patient never suffered with headaches, rhinitis, conjunctivitis, or urticaria.

She was in good health and entirely free from asthmatic symptoms while not pregnant. The patient suffered asthmatic attacks with each pregnancy.

Physical, including the obstetric examination was essentially negative except for the usual respiratory findings in asthmatics.

The remarkable feature of this case was the instantaneous disappearance of all symptoms following the artificial interruption of pregnancy. The author recommends interruption of pregnancy, provided the attacks are severe.

AUGUST F. DARO.

Turunen, A. O. I.: Mediastinal and Subcutaneous Emphysema During Labor, *Acta Obst. et Gynec. Scandinav.* 14: 76, 1934.

The author reports two cases in which young, healthy primiparas in connection with a normal, not unusually difficult delivery, were affected with subcutaneous emphysema in the upper part of the body and localized chiefly on the right side. In one of the cases the thoracic cavity was examined roentgenologically, and for the first time in a case of subcutaneous emphysema, air was shown to be present also in the mediastinum. Clinically it was proved that complete cardiac dullness had disappeared for several days. This testifies that, besides the subcutaneous emphysema appearing in connection with delivery, there is also present a mediastinal emphysema probably due to a subpleural pulmonary rupture. It is, therefore, presumable that the air in such cases wanders from the place of the pulmonary rupture into the mediastinum and from there finally under the skin.

As this complication is very rare and nothing seems necessary for evoking it except the usual great exertion at delivery, it must be presumed that its origin is promoted by congenital anomalies in the respiratory ducts or abnormal friability of the pulmonary tissues. Cases of mediastinal emphysema may occur in connection with delivery oftener than is believed, developing in exceptional cases to such an extent as to lead to subcutaneous emphysema.

J. P. GREENHILL.

Schroeder, C.: Physiology of Respiration During Pregnancy, Klin. Wchnschr. 12: 2067, 1933.

The author studied respiratory movements and pulmonary efficiency during pregnancy and the puerperium in a series of women by means of the pneumotachograph. He found that the respiratory mechanism remains normal throughout pregnancy with a constantly increasing respiratory rate and efficiency. This increase begins in the second month and continues until the end of pregnancy, and varies from 20 to 240 per cent. The return to normal is rapid during the puerperium.

RALPH A. REIS.

Rordorf, Roberto: Transplacental Passage of the Tubercle Bacillus Studied by the Löwenstein Method, Arch. di ostet. e ginec. 20: 627, 1933.

Study of 15 tuberculous women during labor, with active lesions, gave the following results: (1) The tubercle bacillus could not be found in the blood during labor by the cultural method of Löwenstein. (2) Blood from the cord of babies born of these same mothers also gave negative results. (3) The inoculation of guinea pigs with blood also gave only negative results. He concludes from his experiments that the tubercle bacillus does not pass through the placenta.

JAMES M. PIERCE.

Palanos Costa, N., and Falsia, M.: Transplacental Transmission of Tuberculosis, Rev. Soc. argent. de biol. 10: 207, 1934.

The authors obtained amniotic fluid from pregnant women frankly infected with pulmonary tuberculosis by abdominal puncture. The fluid was injected into guinea pigs. Out of 24 cases there was a positive guinea pig autopsy of tuberculosis in 12.5 per cent. Of 21 placentas obtained from pregnant women infected with pulmonary tuberculosis, 4.76 per cent gave positive guinea pig diagnosis of tuberculosis. It is concluded that it is possible to encounter an infected amniotic fluid with sound placenta, and vice versa.

MARIO A. CASTALLO.

Schultze-Rhonhof and Hansen: Critical Analysis of the Question "Tuberculosis and Pregnancy," Med. Klin. 29: 765, 1933.

The prevailing opinion is that active pulmonary tuberculosis is generally aggravated by pregnancy, a latent process is frequently activated and in such cases the pregnancy should be terminated early. However, this opinion is based upon scientific knowledge not as helpful as is available today. With proper medical attention pregnant women with tuberculosis may safely go through gestation. Even in Russia, where abortions are legal, and therefore there is no hesitancy about doing them, obstetricians have in recent years treated tuberculous pregnant women conservatively.

There is no doubt that pregnancy can aggravate the process but this is not the rule. The fate of a woman depends not upon the fact that she is pregnant but upon

the character of the lesion and upon the care she receives during pregnancy. Proper management of these patients lately has been considerably aided by lung surgery in the form of artificial pneumothorax, thoracoplasty, etc. These operations not only permit the continuation of the gestation but also have a favorable effect on the tuberculous process.

In the decision to perform a therapeutic abortion the social aspect must be considered. The problem of tuberculosis and pregnancy like the problem of tuberculosis in general is not only a medical but also a social problem.

The general outlook for babies born of tuberculous mothers is good. Thus in Blisnjanskaja's series of 23,000 children of tuberculous parents, raised in the country, only 7 became diseased. Intrauterine transplacental infection is extremely rare. The important thing is to avoid infection of the child after birth and this requires special care.

J. P. GREENHILL.

Falkiner and Micks: Artificial Pneumothorax and Pregnancy, Irish J. Med. Sc., page 265, 1933.

The authors record a case of successful pregnancy in a patient undergoing treatment by artificial pneumothorax for pulmonary tuberculosis.

Physicians see a relationship between pregnancy and phthisis in two ways. First, a previously dormant tuberculous lesion very often becomes active during the later months of pregnancy or very soon after a confinement. Such processes tend to be far more rapid in their evolution than in the nonpregnant patient. It is most important, therefore, that whenever pulmonary tuberculosis is suspected during pregnancy or after the puerperium an early diagnosis should be made with the object of instituting collapse therapy before the lesions have become extensively bilateral.

The second way in which the relationship obtrudes itself on the notice of the physician is by the problem of advising on the marriage of a patient actually under treatment for pulmonary tuberculosis. Should marriage and childbearing be postponed until after collapse therapy is over and done with (failing the eugenetically ideal course of forbidding marriage altogether)? A phthisical woman should not become pregnant, but if the patient rejects this advice, there may be advantages in allowing the pregnancy to occur while artificial pneumothorax is maintained, rather than waiting until reexpansion is permitted. There is a priori support for this contention, but the question cannot be decided without further evidence.

WM. C. HENSKE.

Larrea, Ricardo: Laryngeal Tuberculosis and Pregnancy, Rev. españ. de obst. y gynec. 46: 479, 1933.

From his study of laryngeal tuberculosis and pregnancy, Larrea concludes: (1) Tuberculosis does not cause sterility. (2) The prognosis is not always fatal since in cases with early lesions the process can be checked and later cured by adequate treatment. (3) The prognosis depends principally upon the general condition of the patient, but above all upon the form and evolution of the pulmonary lesions; the graver the pulmonary lesions, the less the probability of cure of the laryngeal involvement. (4) There should be sanatoria or special departments in hospitals for tuberculous pregnant women where they may be carefully observed during pregnancy. (5) The interruption of pregnancy should be the exception rather than the rule. (6) Labor should be terminated by forceps as soon as feasible to avoid the exertion of the expulsive stage.

JAMES M. PIERCE.

Seitz, L.: Essential Pregnancy Hypertension as a Distinct Entity, Monatschr. f. Geburtsh. u. Gynäk. 97: 325, 1934.

There occurs in some cases a distinct elevation of blood pressure during pregnancy and disappearance of this hypertension during the puerperium, without other apparent symptoms. This the author calls essential pregnancy hypertension. It is particularly noticeable at the end of gestation and during labor and is due to increased work to be performed by the circulatory system. The cause lies in a hormonal and neurologic basis, the diminution in cholin and increase in posterior pituitary hormone in the blood play a distinct rôle. Women who have goiter are particularly prone to develop this type of hypertension. The elevation in blood pressure may lead to disturbances in such parenchymatous organs as kidneys, liver, brain, etc. A hypertension which exists before pregnancy, as a rule, is aggravated by it. When the blood pressure rises above 250 mm. and decompensation disturbances arise, gestation must be interrupted.

J. P. GREENHILL.

Schroeder, Carl: Work of the Heart in Pregnancy, Arch. f. Gynäk. 150: 1, 1932.

The question of cardiac hypertrophy in pregnancy is still a moot one. The blood volume is but slightly increased while the speed of circulation is definitely decreased. The venous pressure remains practically unchanged. The general body metabolism is, however, markedly increased throughout pregnancy.

The author used the Grollman acetylene method for studying the cardiac output, heart minute-volume and investigated the arteriovenous differences in carbon dioxide tension by gas analyses. He finds a definite increase in the circulation during pregnancy due to an average increase of 27 per cent in the cardiac minute-volume. This latter increase is due to a definite and marked increase in cardiac rate in spite of a decrease in the cardiac output of each individual, cardiac contraction. This latter phenomenon is not due to a cardiac dilatation but is most probably caused by some degree of cardiac hypertrophy.

RALPH A. REIS.

Krukenberg, H.: The Influence of Physical Labor on the Heart and Circulation During Pregnancy, Arch. f. Gynäk. 149: 662, 1932.

The roentgen shadow of the heart in pregnancy becomes smaller following physical exertion. This decrease takes place in the longitudinal and transverse diameters as well as in heart volume. No cardiac enlargement was found in any of the patients studied in this series. The blood pressure of pregnant women rises rapidly following physical effort. It rises higher in pregnant than in nonpregnant women. The return to normal is much slower in the presence of pregnancy, especially in older women. The minute-volume of the heart is increased during pregnancy and here also the return to normal is slower in the presence of a pregnancy. When cardiac disease is present, the above changes become more marked.

RALPH A. REIS.

De Maria, Giorgio: The Alkaline Reserve in the Pregnant Cardiopathic Woman, Clin. ostet. 12: 645, 1933.

After repeated determination of the alkaline reserve in cardiopathic pregnant women before, during, and after labor, the author arrives at the following conclusions: (1) In the complicated cardiopathies the alkaline reserve is always diminished; the lower alkaline reserves are found in the grave cardiopathies with decompensation. (2) The lowering of the alkaline reserve is accentuated during

labor. (3) The alkaline reserve generally tends to return to its normal value in the puerperium. The promptness of alkaline reserve to return to normal is in direct proportion to the gravity of the cardiac condition. (4) Repeated alkaline reserve test in the pregnant cardiopathic before, during and after labor may be helpful in prognosis.

AUGUST F. DARO.

Item

American Gynecological Society

The Sixtieth Annual Meeting of the American Gynecological Society will be held in Hot Springs, Virginia, May 27, 28, and 29, 1935.

American Board of Obstetrics and Gynecology

The general examination for all candidates for certification by this Board will be held in the Atlantic City General Hospital on Monday, June 10 and Tuesday, June 11, 1935, immediately prior to the scientific session of the American Medical Association.

Applications for Group A candidates must be received not later than May 1, 1935.

The annual informal dinner and general conference of Diplomates attending the American Medical Association convention will be held at the Traymore Hotel, Atlantic City, Wednesday, June 12 at 7 P.M. At this dinner the successful candidates from the examinations of the two preceding days will be presented in person, and short addresses will be made by several members of the Board.

For further information, booklets, and application blanks apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, (6) Pennsylvania.

Errata

In Table II of Dr. L. A. Emge's paper, page 691 of the November, 1934, issue, the reference to von Graff, 1914, should read "sarcoma in rats" instead of "carcinoma in mice."

In Table II of Dr. Torrance's article on page 437 of the March issue, the first subheading should read:

Comparison of Reaction in Rabbits Before, During, and After
Pregnancy, With Virgin Animals

The heading for the second part of the table should read:

Unmated Controls